UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,460	11/24/2003	Shigeo Ohno	2352.002	6486

23405 7590 10/20/2006

HESLIN ROTHENBERG FARLEY & MESITI PC
5 COLUMBIA CIRCLE
ALBANY, NY 12203

EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/720,460	OHNO, SHIGEO	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2005 and 03 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-20* is/are pending in the application.

4a) Of the above claim(s) *4-14,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,16,17 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/9/04, 8/3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendices A, B, C*.

DETAILED ACTION

Status of the Application

[1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[2] Claims 1-14 and 16-20 are pending in the application.

[3] Applicant's amendment to the claims, filed 5 December 2005 is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[4] Receipt of an information disclosure statement, filed 3 August 2006, in response to a request for information under 37 CFR 1.105, mailed 17 February 2006, is acknowledged.

Election/Restriction

[5] Applicant's election without traverse of Group I, claims 1-3 and 16-17, in the reply filed on 12/5/2005, is acknowledged.

[6] Claims 4-14 and 18-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

[7] Claims 1-3, 16-17, and newly added claim 20, which depends from claim 16, are being examined on the merits. Claims 16-17 have been examined only to the extent the claims read on the elected subject matter.

Claim to Domestic and Foreign Priority

[8] Applicants' claim to domestic priority under 35 U.S.C. § 120 to PCT/JP01/10234, filed 22 November 2001, is acknowledged. Applicant's claim to foreign priority under 35 U.S.C. § 119(a)-(d) to Japanese application JP 2001-156088, having the priority date of 24 May 2001, is acknowledged. A certified copy of the foreign priority document has been filed in the instant application.

Information Disclosure Statement

[9] With the exception of reference CC of the IDS filed 9 August 2004, all references cited in the IDSs filed 9 August 2004 and 3 August 2006 have been considered by the examiner. A copy of Forms PTO-1449 is attached to the instant Office action. Reference CC of the IDS filed 9 August 2004 is lined through as this citation is a duplicate of reference CC of the IDS filed 3 August 2006.

Specification/Informalities

[10] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: --Human SMG-1 Polypeptide--.

Claim Objection(s)

[11] Claims 1 and 16 are objected to in the recitation of "SMG-1." Abbreviations, unless otherwise obvious and/or commonly used in the art, should not be recited in the

claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required.

[12] Claim 1 is objected to as using a confusing format. The claim lists parts (1) and (2) and it is unclear as to whether applicant intends for parts (1) and (2) to be jointly included in claim 1 or whether parts (1) and (2) are intended as being separate claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[13] Claim(s) 16 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "SMG-1 mutant" in claim 16 (claim 20 dependent therefrom) is a relative term which renders the claim indefinite as there is no indication in the claims or the specification as the sequence(s) of an SMG-1 polypeptide or polypeptides that applicant considers to be “non-mutant” and/or “mutant” such that a skilled artisan would have a reference sequence or sequences in order to make a determination of those polypeptides that are considered to be “mutant” SMG-1 polypeptides and those that are considered to be “non-mutant.” As such, it is unclear as to the scope of SMG-1 polypeptides that are encompassed by the claim. In the interest of advancing

prosecution, the examiner has interpreted the term as encompassing any polypeptide variants of SEQ ID NO:2, including those that maintain SMG-1 activity.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[14] Claims 1-3 and 16-17 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to polypeptides or agents. The claims read on a product of nature and should be amended to indicate the hand of the inventor, e.g., by insertion of "purified" or "isolated". See MPEP § 2105.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[15] Claims 16 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" (MPEP 8th Ed., October 2006 Revision at pp. 2100-176 and 2100-183) and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description."

Claim 16 (claim 20 dependent therefrom) has been amended on 5 December 2005 to delete the term "activity-deficient," thus broadening the scope of claimed agents for suppressing nonsense-mediated mRNA decay to comprising any SMG-1 mutant. In the response accompanying the amendment, applicant fails to show support for the amendment to claim 16. While the examiner can find support for an agent for suppressing nonsense-mediated mRNA decay comprising an *activity-deficient* SMG-1 mutant, the examiner can find no support for an agent for suppressing nonsense-mediated mRNA decay to comprising *any* SMG-1 mutant. Applicant is invited to show support for the claim limitation at issue.

[16] Claims 1-2, 16-17, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention. This is a written description rejection.

Claim 1 (claim 17 dependent therefrom) is drawn to (in relevant part) a genus of polypeptides having SMG-1 activity and comprising any variant of amino acids 129 to 3657 of SEQ ID NO:2. Claim 2 is drawn to (in relevant part) a genus of polypeptides having SMG-1 activity and comprising a polypeptide having at least 90% homology (interpreted as meaning identity) to amino acids 129-3657 of SEQ ID NO:2, amino acids 1-3657 of SEQ ID NO:2, or amino acids 107-3657 of SEQ ID NO:2. The specification defines "SMG-1 activity" as "an activity of phosphorylating Upf1/SMG-2 [Sun, X. et al., Proc. Natl. Acad. Sci. USA, 95, 10009-10014 (1998); and Bhattacharya, A. et al., RNA, 6, 1226-1235 (2000)]" (specification at p. 6, lines 17-20). Claims 16 and 20 are drawn to (in relevant part) an agent for suppressing nonsense-mediated mRNA decay comprising a genus of SMG-1 mutants having any structure and any activity and optionally further comprising any aminoglycoside antibiotic having any structure ["aminoglycoside antibiotic" is defined in the specification as being "not particularly limited, so long as it has a nonsense suppression activity alone," specification at p. 34, 2nd full paragraph].

The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by

actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single species of the genus of polypeptides of claims 1-2, *i.e.,* SEQ ID NO:2, and only a single species of the genus of recited polypeptides of claim 16, *i.e.,* SEQ ID NO:2 with a single mutation, wherein the mutation is Asp at position 2331 replaced with Ala [specification at p. 34, 3rd full paragraph]. Other than this single representative species, the specification fails to disclose any other additional representative species of the genus of claimed polypeptides. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus," it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." In the instant case, the claimed genus of polypeptides of claims 1-2 encompasses species that are widely variant with respect to structure [because the genus of polypeptides is limited to those having "SMG-1 activity" as defined above, the genus is not considered to have widely variant functions] and the genus of polypeptides of claim 16

encompasses species that are widely variant with respect to structure *and* function. As such, the disclosure of the single representative species of polypeptides of claims 1-2, *i.e.,* SEQ ID NO:2 or single representative species of polypeptides of claim 16, *i.e.,* SEQ ID NO:2 with a single mutation, wherein the mutation is an Asp to Ala mutation at position 2331, is insufficient to be representative of the attributes and features of all species encompassed by the claimed genus of claimed or recited polypeptides.

Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[17] Claims 1-2, 16-17, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO:2, does not reasonably provide enablement for all variants of SEQ ID NO:2, including SEQ ID NO:2 with a single mutation, wherein the mutation is an Asp to Ala mutation at position 2331, broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows:

(A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claim 1 (claim 17 dependent therefrom) is drawn to (in relevant part) all polypeptides having SMG-1 activity and comprising any variant of SEQ ID NO:2. Claim 2 is drawn to (in relevant part) all polypeptides having SMG-1 activity and comprising a polypeptide having at least 90% homology (interpreted as meaning identity) to amino acids 129-3657 of SEQ ID NO:2, amino acids 1-3657 of SEQ ID NO:2, or amino acids 107-3657 of SEQ ID NO:2. It is noted that the specification defines "SMG-1 activity" as "an activity of phosphorylating Upf1/SMG-2 [Sun, X. et al., Proc. Natl. Acad. Sci. USA, 95, 10009-10014 (1998); and Bhattacharya, A. et al., RNA, 6, 1226-1235 (2000)]" (specification at p. 6, lines 17-20). Claims 16 and 20 are drawn to

(in relevant part) an agent for suppressing nonsense-mediated mRNA decay comprising any SMG-1 mutant having any sequence of amino acids and any activity and optionally further comprising any aminoglycoside antibiotic having any structure ["aminoglycoside antibiotic which may be used in the pharmaceutical composition of the present invention for suppressing nonsense is not particularly limited, so long as it has a nonsense suppression activity alone," specification at p. 34, 2nd full paragraph]. The enablement provided by the specification is not commensurate in scope with the claims with regard to broad scope of polypeptides encompassed by the claims. In this case, the specification is enabling only for the polypeptide of SEQ ID NO:2.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The amino acid sequence of a polypeptide determines the polypeptide's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.*, multiple substitutions. At the time of the invention, methods for isolating or

generating variants of a given polypeptide acid were known in the art. However, neither the specification nor the state of the art at the time of the invention provide the necessary guidance for altering the polypeptide of SEQ ID NO:2 with an expectation of obtaining a polypeptide having the desired activity/utility. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, in the "Introduction to Protein Structure," [Branden and Tooze, Garland Publishing Inc., New York], it is disclosed that "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The cited teachings of "Introduction to Protein Structure" are exemplified by the reference of Witkowski et al. [*Biochemistry* (1999) 38:11643-11650], which teaches that only a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see *e.g.*, Table 1, page 11647).

The amount of direction provided by the inventor and The existence of working examples: The specification discloses how to make and use only a single working example of the claimed polypeptide, *i.e.,* SEQ ID NO:2. While it is acknowledged that the specification discloses a SEQ ID NO:2 variant, *i.e.,* SEQ ID NO:2 with a single mutation, wherein the mutation is an Asp to Ala mutation at position 2331, it is unclear

as to how a skilled artisan is to use this disclosed polypeptide. Other than the single working example of SEQ ID NO:2, the specification fails to disclose any specific guidance for altering the amino acid sequence of SEQ ID NO:2 with an expectation that the resulting variants of SEQ ID NO:2 as encompassed by the claims will achieve or maintain the desired activity/utility.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating or generating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen – by a trial and error process – for all polypeptide variants having a substantial number of modifications as encompassed by the claims for those polypeptides having the desired activity/utility.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability, and the quantity of experimentation, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly,

extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

[18] Claims 1-2 and 16-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Denning et al. [*J Biol Chem* (2001) 276:22709-22714; cited as reference CG in the IDS filed 9 August 2004] as evidenced by GenBank Accession Number AY014957. Applicant's attention is directed to the upper right-hand corner of page 22709 of Denning et al., which states, "[p]ublished, JBC Papers in Press, April 30, 2001." According to the "JBC Papers in Press" website (www.jbc.org/pips/index.dtl; viewed on February 13, 2006), "***JBC Papers in Press***...will establish publication priority" (emphasis in original).

Initially, it is noted that claim 2 recites "a 90% or more homology," wherein the term "homology" is defined in the specification as "a value obtained by BLAST [Basic

local alignment search tool; Altschul, S. F. et al., J. Mol. Biol., 215, 403-410, (1990)]" (specification at p. 16, top). As BLAST can be used to determine *similarity* between two sequences, in accordance with MPEP 2111.01, which states (in relevant part), "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow," the term "homology" has been interpreted as similarity between two sequences.

The claims are drawn to variants of SEQ ID NO:2 having SMG-1 activity (claims 1-2), an agent thereof (claim 17), and an agent for suppressing NMD comprising an SMG-1 mutant (claim 16).

Denning et al. teaches isolation of an SMG-1 polypeptide, which has the ability to phosphorylate Upf1p (p. 22713, Figure 4) or kinase-deficient SMG-1 mutants (p. 22710, right column, middle) and teaches the GenBank Accession Number of the encoding nucleic acid, *i.e.,* AY014957 (p. 22709, bottom, left). The polypeptide encoded by Accession Number AY014957 is 99.7% similar to SEQ ID NO:2 (see Appendix A).

This anticipates claims 1-2 and 16-17 as written.

While it is acknowledged that Denning et al. does not teach the polypeptide as being useful for "suppressing nonsense-mediated mRNA decay" or for "promoting nonsense-mediated mRNA decay," it is noted that if the prior art structure is capable of performing the intended use, then it meets the claim. See MPEP 2111.02.II.

[19] Claims 1-3 and 16-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Ohnishi et al. ("23rd Annual Meeting of the Molecular Biology Society of Japan,"

Program and Abstracts, December 14, 2000; cited as reference CB in the IDS filed 9 August 2004).

Claims 1-2 and 16-17 are drawn to polypeptides and agents as described above. Claim 3 is drawn to a polypeptide consisting of SEQ ID NO:2.

The reference of Ohnishi et al. teaches cloning of a human SMG-1 polypeptide (Figure 1A) isolated from HeLa cells that is 400 or 430 kDa (Figure 3 and description thereof), which is disclosed as having kinase activity (Figure 4 and description thereof). A visual comparison of the sequences of SMG-1 as reported by Ohnishi et al. and SEQ ID NO:2 herein indicates that the sequences are identical. This anticipates claims 1-3 and 16-17 as written.

While it is acknowledged that Ohnishi et al. does not teach the polypeptide as being useful for "suppressing nonsense-mediated mRNA decay" or for "promoting nonsense-mediated mRNA decay," it is noted that if the prior art structure is capable of performing the intended use, then it meets the claim. See MPEP 2111.02.II. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[20] Claims 1-3 and 16-17 are rejected under 35 U.S.C. 102(a) as being anticipated by Yamashita et al. (*Genes Develop* 15:2215-2228, 2001; cited as reference CH in the IDS filed 9 August 2004).

Claims 1-3 and 16-17 are drawn to polypeptides and agents as described above.

The reference of Yamashita et al. teaches cloning of a human SMG-1 polypeptide (Figure 1A) isolated from HeLa cells that is 430 kDa (p. 2218, left column, top), which is disclosed as having kinase activity (p. 2218, right column, bottom). The polypeptide of Yamashita et al. is 100% identical to SEQ ID NO:2 herein (see Appendix B). This anticipates claims 1-3 and 16-17 as written.

While it is acknowledged that Ohnishi et al. does not teach the polypeptide as being useful for "suppressing nonsense-mediated mRNA decay" or for "promoting nonsense-mediated mRNA decay;" it is noted that if the prior art structure is capable of performing the intended use, then it meets the claim. See MPEP 2111.02.II. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[21] Claims 1-3 and 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohnishi et al. ("22nd Annual Meeting of the Molecular Biology Society of Japan,"

Program and Abstracts, December 7-10, 1999; cited as reference CC in the IDS filed 3 August 2006).

Claims 1-3 and 16-17 are drawn to polypeptides and agents as described above.

The reference of Ohnishi et al. teaches immunoprecipitation of a polypeptide referred to as "LICK" from HeLa cell extract (slide 2, part B), which is identified by the reference as being 400 or 430 kDa having kinase activity (abstract) and having an internal sequence that is 100% identical to amino acids 2331 to 2356 of SEQ ID NO:2 herein. This anticipates claims 1-3 and 16-17 as written.

While it is acknowledged that Ohnishi et al. does not teach the entire sequence of LICK, applicant's attention is directed to MPEP 2112, wherein the Court in *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, held that "the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that 'just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.'" In this case, the polypeptide of Ohnishi et al. and the polypeptide of SEQ ID NO:2 are both disclosed *inter alia* as being isolated from HeLa cells, being 400 or 430 kDa, having kinase activity, and having an identical internal sequence as noted above (pp. 48-49 and 57-58 and sequence listing for SEQ ID NO:2). As such, it is the examiner's position that the polypeptide of Ohnishi et al. is SEQ ID NO:2. If applicant traverses the instant rejection on the grounds that Ohnishi et al. does not demonstrate that the disclosed polypeptide

has "SMG-1 activity" as defined in the specification (p. 6, lines 17-20), it is noted that this is an inherent feature of the polypeptide of Ohnishi et al. Also, while it is acknowledged that Ohnishi et al. does not teach the polypeptide as being useful for "suppressing nonsense-mediated mRNA decay" or for "promoting nonsense-mediated mRNA decay," it is noted that if the prior art structure is capable of performing the intended use, then it meets the claim. See MPEP 2111.02.II. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

[22] Claims 1-2 and 16-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Loughney et al. (US Patent 6,344,549).

The claims are drawn to polypeptides and agents as described above.

Loughney et al. teaches isolation of a kinase polypeptide, SEQ ID NO:2, which has 99.9% similarity to SEQ ID NO:2 herein (see Appendix C). Loughney et al. teaches the polypeptide is most closely related to *C. elegans* SMG-1 (column 32).

This anticipates claims 1-2 and 16-17 as written.

If applicant traverses the instant rejection on the grounds that Loughney et al. does not demonstrate that the disclosed polypeptide has "SMG-1 activity" as defined in

the specification (p. 6, lines 17-20), it is noted that this is an inherent feature of the polypeptide of SEQ ID NO:2 of Loughney et al. Also, while it is acknowledged that Loughney et al. does not teach the polypeptide as being useful for "suppressing nonsense-mediated mRNA decay" or for "promoting nonsense-mediated mRNA decay," it is noted that if the prior art structure is capable of performing the intended use, then it meets the claim. See MPEP 2111.02.II. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Conclusion

[23] Status of the claims:

Claims 1-14 and 16-20 are pending.

Claims 4-14 and 18-19 are withdrawn from consideration.

Claims 1-3, 16-17, and 20 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Thursday, 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656

APPENDIX A

```
AY014957
LOCUS       AY014957               11036 bp    mRNA    linear   PRI 18-JUN-2001
DEFINITION  Homo sapiens PI-3-kinase-related kinase SMG-1 (SMG1) mRNA, complete
            cds.
ACCESSION   AY014957
VERSION     AY014957.1  GI:14132743
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (bases 1 to 11036)
  AUTHORS   Denning,G., Jamieson,L., Maquat,L.E., Thompson,E.A. and Fields,A.P.
  TITLE     Cloning of a novel phosphatidylinositol kinase-related kinase:
            characterization of the human SMG-1 RNA surveillance protein
  JOURNAL   J. Biol. Chem. 276 (25), 22709-22714 (2001)
   PUBMED   11331269
REFERENCE   2  (bases 1 to 11036)
  AUTHORS   Denning,G., Jamieson,L. and Fields,A.P.
  TITLE     Direct Submission
  JOURNAL   Submitted (28-NOV-2000) Human Biological Chemistry and Genetics,
            The University of Texas Medical Branch, 301 University Blvd.,
            Galveston, TX 77555, USA
FEATURES             Location/Qualifiers
     source          1. .11036
                     /organism="Homo sapiens"
                     /mol_type="mRNA"
                     /db_xref="taxon:9606"
     gene            1. .11036
                     /gene="SMG1"
     CDS             133. .9228
                     /gene="SMG1"
                     /note="similar to Caenorhabditis elegans nonsense-mediated
                     mRNA decay protein SMG-1; hSMG-1"
                     /codon_start=1
                     /product="PI-3-kinase-related kinase SMG-1"
                     /protein_id="AAK00511.1"
                     /db_xref="GI:14132744"
                     /translation="MWALSPTVFALLSKNLMIVHSDLAVHFPAIQYAVLYTLYSHCTR
                     HDHFISSSLSSSSPSLFDGAVISTVTTATKKHFSIILNLLGILLKKDNLNQDTRKLLM
                     TWALEAAVLMKKSETYAPLFSLPSFHKFCKGLLANTLVEDVNICLQACSSLHALSSSL
                     PDDLLQRCVDVCRVQLVHSGTRIRQAFGKLLKSIPLDVVLSNNNHTEIQEISLALRSH
                     MSKAPSNTFHPQDFSDVISFILYGNSHRTGKDNWLERLFYSCQRLDKRDQSTIPRNLL
                     KTDAVLWQWAIWEAAQFTVLSKLRTPLGRAQDTFQTIEGIIRSLAAHTLNPDQDVSQW
                     TTADNDEGHGNNQLRLVLLLQYLENLEKLMYNAYEGCANALTSPPKVIRTFFYTNRQT
                     CQDWLTRIRLSIMRVGLLAGQPAVTVRHGFDLLTEMKTTSLSQGNELEVTIMMVVEAL
                     CELHCPEAIQGIAVWSSSIVGKNLLWINSVAQQAEGRFEKASVEYQEHLCAMTGVDCC
                     ISSFDKSVLTLANAGRNSASPKHSLNGESRKTVLSKPTDSSPEVINYLGNKACECYIS
                     IADWAAVQEWQNAIHDLKKSTSSTSLNLKADFNYIKSLSSFESGKFVECTEQLELLPG
                     ENINLLAGGSKEKIDMKKLLPNMLSPDPRELQKSIEVQLLRSSVCLATALNPIEQDQK
                     WQSITENVVKYLKQTSRIAIGPLRLSTLTVSQSLPVLSTLQLYCSSALENTVSNRLST
                     EDCLIPLFSEALRSCKQHDVRPWMQALRYTMYQNQLLEKIKEQTVPIRSHLMELGLTA
                     AKFARKRGNVSLATRLLAQCSEVQLGKTTTAQDLVQHFKKLSTQGQVDEKWGPELDIE
                     KTKLLYTAGQSTHAMEMLSSCAISFCKSVKAEYAVAKSILTLAKWIQAEWKEISGQLK
                     QVYRAQHQQNFTGLSTLSKNILTLIELPSVNTMEEEYPRIESESTVHIGVGEPDFILG
                     QLYHLSSVQAPEVAKSWAALASWAYRWGRKVVDNASQGEGVRLLPREKSEVQNLLPDT
                     ITEEEKERIYGILGQAVCRPAGIQDEDITLQITESEDNEEDDMVDVIWRQLISSCPWL
                     SELDESATEGVIKVWRKVVDRIFSLYKLSCSAYFTFLKLNAGQIPLDEDDPRLHLSHR
                     VEQSTDDMIVMATLRLLRLLVKHAGELRQYLEHGLETTPTAPWRGIIPQLFSRLNHPE
                     VYVRQSICNLLCRVAQDSPHLILYPAIVGTISLSSESQASGNKFSTAIPTLLGNIQGE
                     ELLVSECEGGSPPASQDSNKDEPKSGLNEDQAMMQDCYSKIVDKLSSANPTMVLQVQM
                     LVAELRRVTVLWDELWLGVLLQQHMYVLRRIQQLEDEVKRVQNNNTLRKEEKIAIMRE
                     KHTALMKPIVFALEHVRSITAAPAETPHEKWFQDNYGDAIENALEKLKTPLNPAKPGS
                     SWIPFKEIMLSLQQRAQKRASYILRLEEISPWLAAMTNTEIALPGEVSARDTVTIHSV
                     GGTITILPTKTKPKKLLFLGSDGKSYPYLFKGLEDLHLDERIMQFLSIVNTMFATINR
```

QETPRFHARHYSVTPLGTRSGLIQWVDGATPLFGLYKRWQQREAALQAQKAQDSYQTP
QNPGIVPRPSELYYSKIGPALKTVGLSLDVSRRDWPLHVMKAVLEELMEATPPNLLAK
ELWSSCTTPDEWWRVTQSYARSTAVMSMVGYIIGLGDRHLDNVLIDMTTGEVVHIDYN
VCFEKGKSLRVPEKVPFRMTQNIETALGVTGVEGVFRLSCEQVLHIMRRGRETLLTLL
EAFVYDPLVDWTAGGEAGFAGAVYGGGGQQAESKQSKREMEREITRSLFSSRVAEIKV
NWFKNRDEMLVVLPKLDGSLDEYLSLQEQLTDVEKLQGKLLEEIEFLEGAEGVDHPSH
TLQHRYSEHTQLQTQQRAVQEAIQVKLNEFEQWITHYQAAFNNLEATQLASLLQEIST
QMDLGPPSYVPATAFLQNAGQAHLISQCEQLEGEVGALLQQRRSVLRGCLEQLHHYAT
VALQYPKAIFQKHRIEQWKTWMEELICNTTVERCQELYRKYEMQYAPQPPPTVCQFIT
ATEMTLQRYAADINSRLIRQVERLKQEAVTVPVCEDQLKEIERCIKVFLHENGEEGSL
SLASVIISALCTLTRRNLMMEGAASSAGEQLVDLTSRDGAWFLEELCSMSGNVTCLVQ
LLKQCHLVPQDLDIPNPMEASETVHLANGVYTSLQELNSNFRQIIFPEALRCLMKGEY
TLESMLHELDGLIEQTTDGVPLQTLVESLQAYLRNAAMGLEEETHAHYIDVARLLHAQ
YGELIQPRNGSVDETPKMSAGQMLLVAFDGMFAQVETAFSLLVEKLNKMEIPIAWRKI
DIIREARSTQVNFFDDDNHRQVLEEIFFLKRLQTIKEFFRLCGTFSKTLSGSSSLEDQ
NTVNGPVQIVNVKTLFRNSCFSEDQMAKPIKAFTADFVRQLLIGLPNQALGLTLCSFI
SALGVDIIAQVEAKDFGAESKVSVDDLCKKAVEHNIQIGKFSQLVMNRATVLASSYDT
AWKKHDLVRRLETSISSCKTSLQRVQLHIAMFQWQHEDLLINRPQAMSVTPPPRSAIL
TSMKKKLHTLSQIETSIATVQEKLAALESSIEQRLKWAGGANPALAPVLQDFEATIAE
RRNLVLKESQRASQVTFLCSNIIHFESLRTRTAEALNLDAALFELIKRCQQMCSFASQ
FNSSVSELELRLLQRVDTGLEHPIGSSEWLLSAHKQLTQDMSTQRAIQTEKEQQIETV
CETIQNLVDNIKTVLTGHNRQLGDVKHLLKAMAKDEEAALADGEDVPYENSVRQFLGE
YKSWQDNIQTVLFTLVQAMGQVRSQEHVEMLQEITPTLKELKTQSQSIYNNLVSFASP
LVTDATNECSSPTSSATYQPSFAAAVRSNTGQKTQPDVMSQNARKLIQKNLATSADTP
PSTVPGTGKSVACSPKKAVRDPKTGKAVQERNSYAVSVWKRVKAKLEGRDVDPNRRMS
VAEQVDYVIKEATNLDNLAQLYEGWTAWV"

ORIGIN

Alignment Scores:

Pred. No.:	0	Length:	11036
Score:	15696.50	Matches:	3062
Percent Similarity:	99.71%	Conservative:	4
Best Local Similarity:	99.58%	Mismatches:	2
Query Match:	83.74%	Indels:	7
DB:	8	Gaps:	1

US-10-720-460-2 (1-3657) x AY014957 (1-11036)

```
Qy        590 HisGluAlaPheLysAsnHisValPheAsnValAspAsnAlaLysPheValValLysPhe 609
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 CATGAGGCTTTTAAGAATCATGTGTTCAATGTAGACAATGCAAAATTTGTAGTTAAATTT 60

Qy        610 AspLeuSer----------------------AlaLeuThrThrIleGlyAsnAlaLysAsn 622
              ||||||:::                      ||||||||||||||||||||||||||||
Db         61 GACCTCAATTGACTACAAAATTTGTAGTTAAATTTGACTACAATTGGAAATGCCAAAAAC 120

Qy        623 SerLeuIleGlyMetTrpAlaLeuSerProThrValPheAlaLeuLeuSerLysAsnLeu 642
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TCACTAATAGGGATGTGGGCGCTATCTCCAACTGTCTTTGCACTTCTGAGTAAGAATCTG 180

Qy        643 MetIleValHisSerAspLeuAlaValHisPheProAlaIleGlnTyrAlaValLeuTyr 662
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 ATGATTGTGCACAGTGACCTGGCTGTTCACTTCCCTGCCATTCAGTATGCTGTGCTCTAC 240

Qy        663 ThrLeuTyrSerHisCysThrArgHisAspHisPheIleSerSerSerLeuSerSerAla 682
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||:::
Db        241 ACATTGTATTCTCATTGTACCAGGCATGATCACTTTATCTCTAGTAGCCTCAGTTCTTCC 300

Qy        683 SerProSerLeuPheAspGlyAlaValIleSerThrValThrThrAlaThrLysLysHis 702
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TCTCCTTCTTTGTTTGATGGAGCTGTGATTAGCACTGTAACTACGGCTACAAAGAAACAT 360

Qy        703 PheSerIleIleLeuAsnLeuLeuGlyIleLeuLeuLysLysAspAsnLeuAsnGlnAsp 722
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 TTCTCAATTATATTAAATCTTCTGGGAATATTACTTAAGAAAGATAACCTTAACCAGGAC 420

Qy        723 ThrArgLysLeuLeuMetThrTrpAlaLeuGluAlaAlaValLeuMetArgLysSerGlu 742
```

```
                ||||||||||||||||||||||||||||||||||||||||||||||||:::|||||||||
Db        421 ACGAGGAAACTGTTAATGACTTGGGCTTTGGAAGCAGCTGTTTTAATGAAGAAGTCTGAA 480

Qy        743 ThrTyrAlaProLeuPheSerLeuProSerPheHisLysPheCysLysGlyLeuLeuAla 762
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 ACATACGCACCTTTATTCTCTCTTCCGTCTTTCCATAAATTTTGCAAAGGCCTTTTAGCC 540

Qy        763 AsnThrLeuValGluAspValAsnIleCysLeuGlnAlaCysSerSerLeuHisAlaLeu 782
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 AACACTCTCGTTGAAGATGTGAATATCTGTCTGCAGGCATGCAGCAGTCTACATGCTCTG 600

Qy        783 SerSerSerLeuProAspAspLeuLeuGlnArgCysValAspValCysArgValGlnLeu 802
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 TCCTCTTCCTTGCCAGATGATCTTTTACAGAGATGTGTCGATGTTTGCCGTGTTCAACTA 660

Qy        803 ValHisSerGlyThrArgIleArgGlnAlaPheGlyLysLeuLeuLysSerIleProLeu 822
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 GTGCACAGTGGAACTCGTATTCGACAAGCATTTGGAAAACTGTTGAAATCAATTCCTTTA 720

Qy        823 AspValValLeuSerAsnAsnAsnHisThrGluIleGlnGluIleSerLeuAlaLeuArg 842
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GATGTTGTCCTAAGCAATAACAATCACACAGAAATTCAAGAAATTTCTTTAGCATTAAGA 780

Qy        843 SerHisMetSerLysAlaProSerAsnThrPheHisProGlnAspPheSerAspValIle 862
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 AGTCACATGAGTAAAGCACCAAGTAATACATTCCACCCCCAAGATTTCTCTGATGTTATT 840

Qy        863 SerPheIleLeuTyrGlyAsnSerHisArgThrGlyLysAspAsnTrpLeuGluArgLeu 882
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 AGTTTTATTTTGTATGGGAACTCTCATAGAACAGGGAAGGACAATTGGTTGGAAAGACTG 900

Qy        883 PheTyrSerCysGlnArgLeuAspLysArgAspGlnSerThrIleProArgAsnLeuLeu 902
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TTCTATAGCTGCCAGAGACTGGATAAGCGTGACCAGTCAACAATTCCACGCAATCTCCTG 960

Qy        903 LysThrAspAlaValLeuTrpGlnTrpAlaIleTrpGluAlaAlaGlnPheThrValLeu 922
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 AAGACAGATGCTGTCCTTTGGCAGTGGGCCATATGGGAAGCTGCACAATTCACTGTTCTT 1020

Qy        923 SerLysLeuArgThrProLeuGlyArgAlaGlnAspThrPheGlnThrIleGluGlyIle 942
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 TCTAAGCTGAGAACCCCACTGGGCAGAGCTCAAGACACCTTCCAGACAATTGAAGGTATC 1080

Qy        943 IleArgSerLeuAlaAlaHisThrLeuAsnProAspGlnAspValSerGlnTrpThrThr 962
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 ATTCGAAGTCTCGCAGCTCACACATTAAACCCTGATCAGGATGTTAGTCAGTGGACAACT 1140

Qy        963 AlaAspAsnAspGluGlyHisGlyAsnAsnGlnLeuArgLeuValLeuLeuLeuGlnTyr 982
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 GCAGACAATGATGAAGGCCATGGTAACAACCAACTTAGACTTGTTCTTCTTCTGCAGTAT 1200

Qy        983 LeuGluAsnLeuGluLysLeuMetTyrAsnAlaTyrGluGlyCysAlaAsnAlaLeuThr 1002
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 CTGGAAAATCTGGAGAAATTAATGTATAATGCATACGAGGGATGTGCTAATGCATTAACT 1260

Qy       1003 SerProProLysValIleArgThrPhePheTyrThrAsnArgGlnThrCysGlnAspTrp 1022
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 TCACCTCCCAAGGTCATTAGAACTTTTTTCTATACCAATCGCCAAACTTGTCAGGACTGG 1320

Qy       1023 LeuThrArgIleArgLeuSerIleMetArgValGlyLeuLeuAlaGlyGlnProAlaVal 1042
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 CTAACGCGGATTCGACTCTCCATCATGAGGGTAGGATTGTTGGCAGGCCAGCCTGCAGTG 1380

Qy       1043 ThrValArgHisGlyPheAspLeuLeuThrGluMetLysThrThrSerLeuSerGlnGly 1062
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 ACAGTGAGACATGGCTTTGACTTGCTTACAGAGATGAAAACAACCAGCCTATCTCAGGGG 1440
```

```
Qy       1063 AsnGluLeuGluValThrIleMetMetValValGluAlaLeuCysGluLeuHisCysPro 1082
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 AATGAATTGGAAGTAACCATTATGATGGTGGTAGAAGCATTATGTGAACTTCATTGTCCT 1500

Qy       1083 GluAlaIleGlnGlyIleAlaValTrpSerSerSerIleValGlyLysAsnLeuLeuTrp 1102
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 GAAGCTATACAGGGAATTGCTGTCTGGTCATCATCTATTGTTGGAAAAAATCTTCTGTGG 1560

Qy       1103 IleAsnSerValAlaGlnGlnAlaGluGlyArgPheGluLysAlaSerValGluTyrGln 1122
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 ATTAACTCAGTGGCTCAACAGGCTGAAGGGAGGTTTGAAAAGGCCTCTGTGGAGTACCAG 1620

Qy       1123 GluHisLeuCysAlaMetThrGlyValAspCysCysIleSerSerPheAspLysSerVal 1142
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 GAACACCTGTGTGCCATGACAGGTGTTGATTGCTGCATCTCCAGCTTTGACAAATCGGTG 1680

Qy       1143 LeuThrLeuAlaAsnAlaGlyArgAsnSerAlaSerProLysHisSerLeuAsnGlyGlu 1162
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 CTCACCTTAGCCAATGCTGGGCGTAACAGTGCCAGCCCGAAACATTCTCTGAATGGTGAA 1740

Qy       1163 SerArgLysThrValLeuSerLysProThrAspSerSerProGluValIleAsnTyrLeu 1182
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 TCCAGAAAAACTGTGCTGTCCAAACCGACTGACTCTTCCCCTGAGGTTATAAATTATTTA 1800

Qy       1183 GlyAsnLysAlaCysGluPheTyrIleSerIleAlaAspTrpAlaAlaValGlnGluTrp 1202
             |||||||||||||||||| ||||||||||||||||||||||||||||||||||||||||||
Db       1801 GGAAATAAAGCATGTGAGTGCTACATCTCAATTGCCGATTGGGCTGCTGTGCAGGAATGG 1860

Qy       1203 GlnAsnAlaIleHisAspLeuLysLysSerThrSerSerThrSerLeuAsnLeuLysAla 1222
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 CAGAACGCTATCCATGACTTGAAAAAGAGTACCAGTAGCACTTCCCTCAACCTGAAAGCT 1920

Qy       1223 AspPheAsnTyrIleLysSerLeuSerSerPheGluSerGlyLysPheValGluCysThr 1242
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 GACTTCAACTATATAAAATCATTAAGCAGCTTTGAGTCTGGAAAATTTGTTGAATGTACC 1980

Qy       1243 GluGlnLeuGluLeuLeuProGlyGluAsnIleAsnLeuLeuAlaGlyGlySerLysGlu 1262
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 GAGCAGTTAGAATTGTTACCAGGAGAAAATATCAATCTACTTGCTGGAGGATCAAAAGAA 2040

Qy       1263 LysIleAspMetLysLysLeuLeuProAsnMetLeuSerProAspProArgGluLeuGln 1282
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 AAAATAGACATGAAAAAACTGCTTCCTAACATGTTAAGTCCGGATCCGAGGGAACTTCAG 2100

Qy       1283 LysSerIleGluValGlnLeuLeuArgSerSerValCysLeuAlaThrAlaLeuAsnPro 1302
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 AAATCCATTGAAGTTCAATTGTTAAGAAGTTCTGTTTGTTTGGCAACTGCTTTAAACCCG 2160

Qy       1303 IleGluGlnAspGlnLysTrpGlnSerIleThrGluAsnValValLysTyrLeuLysGln 1322
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 ATAGAACAAGATCAGAAGTGGCAGTCTATAACTGAAAATGTGGTAAAGTACTTGAAGCAA 2220

Qy       1323 ThrSerArgIleAlaIleGlyProLeuArgLeuSerThrLeuThrValSerGlnSerLeu 1342
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 ACATCCCGCATCGCTATTGGACCTCTGAGACTTTCTACTTTAACAGTTTCACAGTCTTTG 2280

Qy       1343 ProValLeuSerThrLeuGlnLeuTyrCysSerSerAlaLeuGluAsnThrValSerAsn 1362
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 CCAGTTCTAAGTACCTTGCAGCTGTATTGCTCATCTGCTTTGGAGAACACAGTTTCTAAC 2340

Qy       1363 ArgLeuSerThrGluAspCysLeuIleProLeuPheSerGluAlaLeuArgSerCysLys 1382
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2341 AGACTTTCAACAGAGGACTGTCTTATTCCACTCTTCAGTGAAGCTTTACGTTCATGTAAA 2400

Qy       1383 GlnHisAspValArgProTrpMetGlnAlaLeuArgTyrThrMetTyrGlnAsnGlnLeu 1402
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2401 CAGCATGACGTGAGGCCATGGATGCAGGCATTAAGGTATACTATGTACCAGAATCAGTTG 2460
```

```
Qy       1403 LeuGluLysIleLysGluGlnThrValProIleArgSerHisLeuMetGluLeuGlyLeu 1422
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2461 TTGGAGAAAATTAAAGAACAAACAGTCCCAATTAGAAGCCATCTCATGGAATTAGGTCTA 2520

Qy       1423 ThrAlaAlaLysPheAlaArgLysArgGlyAsnValSerLeuAlaThrArgLeuLeuAla 1442
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2521 ACAGCAGCAAAATTTGCTAGAAAACGAGGGAATGTGTCCCTTGCAACAAGACTGCTGGCA 2580

Qy       1443 GlnCysSerGluValGlnLeuGlyLysThrThrAlaGlnAspLeuValGlnHisPhe 1462
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2581 CAGTGCAGTGAAGTTCAGCTGGGAAAGACCACCACTGCACAGGATTTAGTCCAACATTTT 2640

Qy       1463 LysLysLeuSerThrGlnGlyGlnValAspGluLysTrpGlyProGluLeuAspIleGlu 1482
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2641 AAAAAACTATCAACCCAAGGTCAAGTGGATGAAAAATGGGGGCCCGAACTTGATATTGAA 2700

Qy       1483 LysThrLysLeuLeuTyrThrAlaGlyGlnSerThrHisAlaMetGluMetLeuSerSer 1502
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2701 AAAACCAAATTGCTTTATACAGCAGGCCAGTCAACACATGCAATGGAAATGTTGAGTTCT 2760

Qy       1503 CysAlaIleSerPheCysLysSerValLysAlaGluTyrAlaValAlaLysSerIleLeu 1522
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2761 TGTGCCATATCTTTCTGCAAGTCTGTGAAAGCTGAATATGCAGTTGCTAAATCAATTCTG 2820

Qy       1523 ThrLeuAlaLysTrpIleGlnAlaGluTrpLysGluIleSerGlyGlnLeuLysGlnVal 1542
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2821 ACACTGGCTAAATGGATCCAGGCAGAATGGAAAGAGATTTCAGGACAGCTGAAACAGGTT 2880

Qy       1543 TyrArgAlaGlnHisGlnGlnAsnPheThrGlyLeuSerThrLeuSerLysAsnIleLeu 1562
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2881 TACAGAGCTCAGCACCAACAGAACTTCACAGGTCTTTCTACTTTGTCTAAAAACATACTC 2940

Qy       1563 ThrLeuIleGluLeuProSerValAsnThrMetGluGluGluTyrProArgIleGluSer 1582
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2941 ACTCTAATAGAACTGCCATCTGTTAATACGATGGAAGAAGAGTATCCTCGGATCGAGAGT 3000

Qy       1583 GluSerThrValHisIleGlyValGlyGluProAspPheIleLeuGlyGlnLeuTyrHis 1602
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3001 GAATCTACAGTGCATATTGGAGTTGGAGAACCTGACTTCATTTTGGGACAGTTGTATCAC 3060

Qy       1603 LeuSerSerValGlnAlaProGluValAlaLysSerTrpAlaAlaLeuAlaSerTrpAla 1622
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3061 CTGTCTTCAGTACAGGCACCTGAAGTAGCCAAATCTTGGGCAGCGTTGGCCAGCTGGGCT 3120

Qy       1623 TyrArgTrpGlyArgLysValValAspAsnAlaSerGlnGlyGluGlyValArgLeuLeu 1642
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3121 TATAGGTGGGGCAGAAAGGTGGTTGACAATGCCAGTCAGGGAGAAGGTGTTCGTCTGCTG 3180

Qy       1643 ProArgGluLysSerGluValGlnAsnLeuLeuProAspThrIleThrGluGluGluLys 1662
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3181 CCTAGAGAAAAATCTGAAGTTCAGAATCTACTTCCAGACACTATAACTGAGGAAGAGAAA 3240

Qy       1663 GluArgIleTyrGlyIleLeuGlyGlnAlaValCysArgProAlaGlyIleGlnAspGlu 1682
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3241 GAGAGAATATATGGTATTCTTGGACAGGCTGTGTGTCGGCCGGCGGGGATTCAGGATGAA 3300

Qy       1683 AspIleThrLeuGlnIleThrGluSerGluAspAsnGluGluAspAspMetValAspVal 1702
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3301 GATATAACACTTCAGATAACTGAGAGTGAAGACAACGAAGAAGATGACATGGTTGATGTT 3360

Qy       1703 IleTrpArgGlnLeuIleSerSerCysProTrpLeuSerGluLeuAspGluSerAlaThr 1722
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3361 ATCTGGCGTCAGTTGATATCAAGCTGCCCATGGCTTTCAGAACTTGATGAAAGTGCAACT 3420

Qy       1723 GluGlyValIleLysValTrpArgLysValValAspArgIlePheSerLeuTyrLysLeu 1742
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db      3421 GAAGGAGTTATTAAAGTGTGGAGGAAAGTTGTAGATAGAATATTCAGCCTGTACAAACTC 3480

Qy      1743 SerCysSerAlaTyrPheThrPheLeuLysLeuAsnAlaGlyGlnIleProLeuAspGlu 1762
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3481 TCTTGCAGTGCATACTTTACTTTCCTTAAACTCAACGCTGGTCAAATTCCTTTAGATGAG 3540

Qy      1763 AspAspProArgLeuHisLeuSerHisArgValGluGlnSerThrAspAspMetIleVal 1782
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3541 GATGACCCTAGGCTGCATTTAAGTCACAGAGTGGAACAGAGCACTGATGACATGATTGTG 3600

Qy      1783 MetAlaThrLeuArgLeuLeuArgLeuLeuValLysHisAlaGlyGluLeuArgGlnTyr 1802
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3601 ATGGCCACATTGCGCCTGCTGCGGTTGCTCGTGAAGCACGCTGGTGAGCTTCGGCAGTAT 3660

Qy      1803 LeuGluHisGlyLeuGluThrThrProThrAlaProTrpArgGlyIleIleProGlnLeu 1822
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3661 CTGGAGCACGGCTTGGAGACAACACCCACTGCACCATGGAGAGGAATTATTCCGCAACTT 3720

Qy      1823 PheSerArgLeuAsnHisProGluValTyrValArgGlnSerIleCysAsnLeuLeuCys 1842
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3721 TTCTCACGCTTAAACCACCCTGAAGTGTATGTGCGCCAAAGTATTTGTAACCTTCTCTGC 3780

Qy      1843 ArgValAlaGlnAspSerProHisLeuIleLeuTyrProAlaIleValGlyThrIleSer 1862
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3781 CGTGTGGCTCAAGATTCCCCACATCTCATATTGTATCCTGCAATAGTGGGTACCATATCG 3840

Qy      1863 LeuSerSerGluSerGlnAlaSerGlyAsnLysPheSerThrAlaIleProThrLeuLeu 1882
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3841 CTTAGTAGTGAATCCCAGGCTTCAGGAAATAAATTTTCCACTGCAATTCCAACTTTACTT 3900

Qy      1883 GlyAsnIleGlnGlyGluGluLeuLeuValSerGluCysGluGlyGlySerProProAla 1902
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3901 GGCAATATTCAAGGAGAAGAATTGCTGGTTTCTGAATGTGAGGGAGGAAGTCCTCCTGCA 3960

Qy      1903 SerGlnAspSerAsnLysAspGluProLysSerGlyLeuAsnGluAspGlnAlaMetMet 1922
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      3961 TCTCAGGATAGCAATAAGGATGAACCTAAAAGTGGATTAAATGAAGACCAAGCCATGATG 4020

Qy      1923 GlnAspCysTyrSerLysIleValAspLysLeuSerSerAlaAsnProThrMetValLeu 1942
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      4021 CAGGATTGTTACAGCAAAATTGTAGATAAGCTGTCCTCTGCAAACCCCACCATGGTATTA 4080

Qy      1943 GlnValGlnMetLeuValAlaGluLeuArgArgValThrValLeuTrpAspGluLeuTrp 1962
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      4081 CAGGTTCAGATGCTCGTGGCTGAACTGCGCAGGGTCACTGTGCTCTGGGATGAGCTCTGG 4140

Qy      1963 LeuGlyValLeuLeuGlnGlnHisMetTyrValLeuArgArgIleGlnGlnLeuGluAsp 1982
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      4141 CTGGGAGTTTTGCTGCAACAACACATGTATGTCCTGAGACGAATTCAGCAGCTTGAAGAT 4200

Qy      1983 GluValLysArgValGlnAsnAsnAsnThrLeuArgLysGluGluLysIleAlaIleMet 2002
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      4201 GAGGTGAAGAGAGTCCAGAACAACAACACCTTACGCAAAGAAGAGAAAATTGCAATCATG 4260

Qy      2003 ArgGluArgHisThrAlaLeuMetLysProIleValPheAlaLeuGluHisValArgSer 2022
             ||||||:::||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      4261 AGGGAGAAGCACACAGCTTTGATGAAGCCCATCGTATTTGCTTTGGAGCATGTGAGGAGT 4320

Qy      2023 IleThrAlaAlaProAlaGluThrProHisGluLysTrpPheGlnAspAsnTyrGlyAsp 2042
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      4321 ATCACAGCGGCTCCTGCAGAAACACCTCATGAAAAATGGTTTCAGGATAACTATGGTGAT 4380

Qy      2043 AlaIleGluAsnAlaLeuGluLysLeuLysThrProLeuAsnProAlaLysProGlySer 2062
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      4381 GCCATTGAAAATGCCCTAGAAAAACTGAAGACTCCATTGAACCCTGCAAAGCCTGGGAGC 4440

Qy      2063 SerTrpIleProPheLysGluIleMetLeuSerLeuGlnGlnArgAlaGlnLysArgAla 2082
```

```
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4441 AGCTGGATTCCATTTAAAGAGATAATGCTAAGTTTGCAACAGAGAGCACAGAAACGTGCA 4500

Qy       2083 SerTyrIleLeuArgLeuGluGluIleSerProTrpLeuAlaAlaMetThrAsnThrGlu 2102
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4501 AGTTACATCTTGCGTCTTGAAGAAATCAGTCCATGGTTGGCTGCCATGACTAACACTGAA 4560

Qy       2103 IleAlaLeuProGlyGluValSerAlaArgAspThrValThrIleHisSerValGlyGly 2122
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4561 ATTGCTCTTCCTGGGGAAGTCTCAGCCAGAGACACTGTCACAATCCATAGTGTGGGCGGA 4620

Qy       2123 ThrIleThrIleLeuProThrLysThrLysProLysLysLeuLeuPheLeuGlySerAsp 2142
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4621 ACCATCACAATCTTACCGACTAAAACCAAGCCAAAGAAACTTCTCTTTCTTGGATCAGAT 4680

Qy       2143 GlyLysSerTyrProTyrLeuPheLysGlyLeuGluAspLeuHisLeuAspGluArgIle 2162
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4681 GGGAAGAGCTATCCTTATCTTTTCAAAGGACTGGAGGATTTACATCTGGATGAGAGAATA 4740

Qy       2163 MetGlnPheLeuSerIleValAsnThrMetPheAlaThrIleAsnArgGlnGluThrPro 2182
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4741 ATGCAGTTCCTATCTATTGTGAATACCATGTTTGCTACAATTAATCGCCAAGAAACACCC 4800

Qy       2183 ArgPheHisAlaArgHisTyrSerValThrProLeuGlyThrArgSerGlyLeuIleGln 2202
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4801 CGGTTCCATGCTCGACACTATTCTGTAACACCACTAGGAACAAGATCAGGACTAATCCAG 4860

Qy       2203 TrpValAspGlyAlaThrProLeuPheGlyLeuTyrLysArgTrpGlnGlnArgGluAla 2222
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4861 TGGGTAGATGGAGCCACACCCTTATTTGGTCTTTACAAACGATGGCAACAACGGGAAGCT 4920

Qy       2223 AlaLeuGlnAlaGlnLysAlaGlnAspSerTyrGlnThrProGlnAsnProGlyIleVal 2242
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4921 GCCTTACAAGCACAAAAGGCCCAAGATTCCTACCAAACTCCTCAGAATCCTGGAATTGTA 4980

Qy       2243 ProArgProSerGluLeuTyrTyrSerLysIleGlyProAlaLeuLysThrValGlyLeu 2262
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       4981 CCCCGTCCTAGTGAACTTTATTACAGTAAAATTGGCCCTGCTTTGAAAACAGTTGGGCTT 5040

Qy       2263 SerLeuAspValSerArgArgAspTrpProLeuHisValMetLysAlaValLeuGluGlu 2282
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5041 AGCCTGGATGTGTCCCGTCGGGATTGGCCTCTTCATGTAATGAAGGCAGTATTGGAAGAG 5100

Qy       2283 LeuMetGluAlaThrProProAsnLeuLeuAlaLysGluLeuTrpSerSerCysThrThr 2302
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5101 TTAATGGAGGCCACACCCCCGAATCTCCTTGCCAAAGAGCTCTGGTCATCTTGCACAACA 5160

Qy       2303 ProAspGluTrpTrpArgValThrGlnSerTyrAlaArgSerThrAlaValMetSerMet 2322
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5161 CCTGATGAATGGTGGAGAGTTACGCAGTCTTATGCAAGATCTACTGCAGTCATGTCTATG 5220

Qy       2323 ValGlyTyrIleIleGlyLeuGlyAspArgHisLeuAspAsnValLeuIleAspMetThr 2342
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5221 GTTGGATACATAATTGGCCTTGGAGACAGACATCTGGATAATGTTCTTATAGATATGACG 5280

Qy       2343 ThrGlyGluValValHisIleAspTyrAsnValCysPheGluLysGlyLysSerLeuArg 2362
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5281 ACTGGAGAAGTTGTTCACATAGATTACAATGTTTGCTTTGAAAAAGGTAAAAGCCTTAGA 5340

Qy       2363 ValProGluLysValProPheArgMetThrGlnAsnIleGluThrAlaLeuGlyValThr 2382
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5341 GTTCCTGAGAAAGTACCTTTTCGAATGACACAAAACATTGAAACAGCACTGGGTGTAACT 5400

Qy       2383 GlyValGluGlyValPheArgLeuSerCysGluGlnValLeuHisIleMetArgArgGly 2402
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5401 GGAGTAGAAGGTGTATTTAGGCTTTCATGTGAGCAGGTTTTACACATTATGCGGCGTGGC 5460
```

```
Qy       2403 ArgGluThrLeuLeuThrLeuLeuGluAlaPheValTyrAspProLeuValAspTrpThr 2422
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5461 AGAGAGACCCTGCTGACGCTGCTGGAGGCCTTTGTGTACGACCCTCTGGTGGACTGGACA 5520

Qy       2423 AlaGlyGlyGluAlaGlyPheAlaGlyAlaValTyrGlyGlyGlyGlyGlnGlnAlaGlu 2442
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5521 GCAGGAGGCGAGGCTGGGTTTGCTGGTGCTGTCTATGGTGGAGGTGGCCAGCAGGCCGAG 5580

Qy       2443 SerLysGlnSerLysArgGluMetGluArgGluIleThrArgSerLeuPheSerSerArg 2462
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5581 AGCAAGCAGAGCAAGAGAGAGATGGAGCGAGAGATCACCCGCAGCCTGTTTTCTTCTAGA 5640

Qy       2463 ValAlaGluIleLysValAsnTrpPheLysAsnArgAspGluMetLeuValValLeuPro 2482
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5641 GTAGCTGAGATTAAGGTGAACTGGTTTAAGAATAGAGATGAGATGCTGGTTGTGCTTCCC 5700

Qy       2483 LysLeuAspGlySerLeuAspGluTyrLeuSerLeuGlnGluGlnLeuThrAspValGlu 2502
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5701 AAGTTGGACGGTAGCTTAGATGAATACCTAAGCTTGCAAGAGCAACTGACAGATGTGGAA 5760

Qy       2503 LysLeuGlnGlyLysLeuLeuGluGluIleGluPheLeuGluGlyAlaGluGlyValAsp 2522
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5761 AAACTGCAGGGCAAACTACTGGAGGAAATAGAGTTTCTAGAAGGAGCTGAAGGGGTGGAT 5820

Qy       2523 HisProSerHisThrLeuGlnHisArgTyrSerGluHisThrGlnLeuGlnThrGlnGln 2542
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5821 CATCCTTCTCATACTCTGCAACACAGGTATTCTGAGCACACCCAACTACAGACTCAGCAA 5880

Qy       2543 ArgAlaValGlnGluAlaIleGlnValLysLeuAsnGluPheGluGlnTrpIleThrHis 2562
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5881 AGAGCTGTTCAGGAAGCAATCCAGGTGAAGCTGAATGAATTTGAACAATGGATAACACAT 5940

Qy       2563 TyrGlnAlaAlaPheAsnAsnLeuGluAlaThrGlnLeuAlaSerLeuLeuGlnGluIle 2582
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       5941 TATCAGGCTGCATTCAATAATTTAGAAGCAACACAGCTTGCAAGCTTGCTTCAAGAGATA 6000

Qy       2583 SerThrGlnMetAspLeuGlyProProSerTyrValProAlaThrAlaPheLeuGlnAsn 2602
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6001 AGCACACAAATGGACCTTGGTCCTCCAAGTTACGTGCCAGCAACAGCCTTTCTGCAGAAT 6060

Qy       2603 AlaGlyGlnAlaHisLeuIleSerGlnCysGluGlnLeuGluGlyGluValGlyAlaLeu 2622
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6061 GCTGGTCAGGCCCACTTGATTAGCCAGTGCGAGCAGCTGGAGGGGGAGGTTGGTGCTCTC 6120

Qy       2623 LeuGlnGlnArgArgSerValLeuArgGlyCysLeuGluGlnLeuHisHisTyrAlaThr 2642
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6121 CTGCAGCAGAGGCGCTCCGTGCTCCGTGGCTGTCTGGAGCAACTGCATCACTATGCAACC 6180

Qy       2643 ValAlaLeuGlnTyrProLysAlaIlePheGlnLysHisArgIleGluGlnTrpLysThr 2662
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6181 GTGGCCCTGCAGTATCCGAAGGCCATATTTCAGAAACATCGAATTGAACAGTGGAAGACC 6240

Qy       2663 TrpMetGluGluLeuIleCysAsnThrThrValGluArgCysGlnGluLeuTyrArgLys 2682
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6241 TGGATGGAAGAGCTCATCTGTAACACCACAGTAGAGCGTTGTCAAGAGCTCTATAGGAAA 6300

Qy       2683 TyrGluMetGlnTyrAlaProGlnProProProThrValCysGlnPheIleThrAlaThr 2702
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6301 TATGAAATGCAATATGCTCCCCAGCCACCCCCAACAGTGTGTCAGTTCATCACTGCCACT 6360

Qy       2703 GluMetThrLeuGlnArgTyrAlaAlaAspIleAsnSerArgLeuIleArgGlnValGlu 2722
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6361 GAAATGACCCTGCAGCGATACGCAGCAGACATCAACAGCAGACTTATTAGACAAGTGGAA 6420

Qy       2723 ArgLeuLysGlnGluAlaValThrValProValCysGluAspGlnLeuLysGluIleGlu 2742
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6421 CGCTTGAAACAGGAAGCTGTCACTGTGCCAGTTTGTGAAGATCAGTTGAAAGAAATTGAA 6480
```

```
Qy       2743 ArgCysIleLysValPheLeuHisGluAsnGlyGluGluGlySerLeuSerLeuAlaSer 2762
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6481 CGTTGCATTAAAGTTTTCCTTCATGAGAATGGAGAAGAAGGATCTTTGAGTCTAGCAAGT 6540

Qy       2763 ValIleIleSerAlaLeuCysThrLeuThrArgArgAsnLeuMetMetGluGlyAlaAla 2782
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6541 GTTATTATTTCTGCCCTTTGTACCCTTACAAGGCGTAACCTGATGATGGAAGGTGCAGCG 6600

Qy       2783 SerSerAlaGlyGluGlnLeuValAspLeuThrSerArgAspGlyAlaTrpPheLeuGlu 2802
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6601 TCAAGTGCTGGAGAACAGCTGGTTGATCTGACTTCTCGGGATGGAGCCTGGTTCTTGGAG 6660

Qy       2803 GluLeuCysSerMetSerGlyAsnValThrCysLeuValGlnLeuLeuLysGlnCysHis 2822
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6661 GAACTCTGCAGTATGAGCGGAAACGTCACCTGCTTGGTTCAGTTACTGAAGCAGTGCCAC 6720

Qy       2823 LeuValProGlnAspLeuAspIleProAsnProMetGluAlaSerGluThrValHisLeu 2842
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6721 CTGGTGCCACAGGACTTAGATATCCCGAACCCCATGGAAGCGTCTGAGACAGTTCACTTA 6780

Qy       2843 AlaAsnGlyValTyrThrSerLeuGlnGluLeuAsnSerAsnPheArgGlnIleIlePhe 2862
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6781 GCCAATGGAGTGTATACCTCACTTCAGGAATTGAATTCGAATTTCCGGCAAATCATATTT 6840

Qy       2863 ProGluAlaLeuArgCysLeuMetLysGlyGluTyrThrLeuGluSerMetLeuHisGlu 2882
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6841 CCAGAAGCACTTCGATGTTTAATGAAAGGGGAATACACGTTAGAAAGTATGCTGCATGAA 6900

Qy       2883 LeuAspGlyLeuIleGluGlnThrThrAspGlyValProLeuGlnThrLeuValGluSer 2902
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6901 CTGGACGGTCTTATTGAGCAGACCACCGATGGCGTTCCCCTGCAGACTCTAGTGGAATCT 6960

Qy       2903 LeuGlnAlaTyrLeuArgAsnAlaAlaMetGlyLeuGluGluGluThrHisAlaHisTyr 2922
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       6961 CTTCAGGCCTACTTAAGAAACGCAGCTATGGGACTGGAAGAAGAAACACATGCTCATTAC 7020

Qy       2923 IleAspValAlaArgLeuLeuHisAlaGlnTyrGlyGluLeuIleGlnProArgAsnGly 2942
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7021 ATCGATGTTGCCAGACTACTACATGCTCAGTACGGTGAATTAATCCAACCGAGAAATGGT 7080

Qy       2943 SerValAspGluThrProLysMetSerAlaGlyGlnMetLeuLeuValAlaPheAspGly 2962
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7081 TCAGTTGATGAAACACCCAAAATGTCAGCTGGCCAGATGCTTTTGGTAGCATTCGATGGC 7140

Qy       2963 MetPheAlaGlnValGluThrAlaPheSerLeuLeuValGluLysLeuAsnLysMetGlu 2982
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7141 ATGTTTGCTCAAGTTGAAACTGCTTTCAGCTTATTAGTTGAAAAGTTGAACAAGATGGAA 7200

Qy       2983 IleProIleAlaTrpArgLysIleAspIleIleArgGluAlaArgSerThrGlnValAsn 3002
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7201 ATTCCCATAGCTTGGCGAAAGATTGACATCATAAGGGAAGCCAGGAGTACTCAAGTTAAT 7260

Qy       3003 PhePheAspAspAspAsnHisArgGlnValLeuGluGluIlePhePheLeuLysArgLeu 3022
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7261 TTTTTTGATGATGATAATCACCGGCAGGTGCTAGAAGAGATTTTCTTTCTAAAAAGACTA 7320

Qy       3023 GlnThrIleLysGluPhePheArgLeuCysGlyThrPheSerLysThrLeuSerGlySer 3042
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7321 CAGACTATTAAGGAGTTCTTCAGGCTCTGTGGTACCTTTTCTAAAACATTGTCAGGATCA 7380

Qy       3043 SerSerLeuGluAspGlnAsnThrValAsnGlyProValGlnIleValAsnValLysThr 3062
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       7381 AGTTCACTTGAAGATCAGAATACTGTGAATGGGCCTGTACAGATTGTCAATGTGAAAACC 7440

Qy       3063 LeuPheArgAsnSerCysPheSerGluAspGlnMetAlaLysProIleLysAlaPheThr 3082
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db      7441 CTTTTTAGAAACTCTTGTTTCAGTGAAGACCAAATGGCCAAACCTATCAAGGCATTCACA 7500

Qy      3083 AlaAspPheValArgGlnLeuLeuIleGlyLeuProAsnGlnAlaLeuGlyLeuThrLeu 3102
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7501 GCTGACTTTGTGAGGCAGCTCTTGATAGGGCTACCCAACCAAGCCCTCGGACTCACACTG 7560

Qy      3103 CysSerPheIleSerAlaLeuGlyValAspIleIleAlaGlnValGluAlaLysAspPhe 3122
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7561 TGCAGTTTTATCAGTGCTCTGGGTGTAGACATCATTGCTCAAGTAGAGGCAAAGGACTTT 7620

Qy      3123 GlyAlaGluSerLysValSerValAspAspLeuCysLysLysAlaValGluHisAsnIle 3142
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7621 GGTGCCGAAAGCAAAGTTTCTGTTGATGATCTCTGTAAGAAAGCGGTGGAACATAACATC 7680

Qy      3143 GlnIleGlyLysPheSerGlnLeuValMetAsnArgAlaThrValLeuAlaSerSerTyr 3162
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7681 CAGATAGGGAAGTTCTCTCAGCTGGTTATGAACAGGGCAACTGTGTTAGCAAGTTCTTAC 7740

Qy      3163 AspThrAlaTrpLysLysHisAspLeuValArgArgLeuGluThrSerIleSerSerCys 3182
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7741 GACACTGCCTGGAAGAAGCATGACTTGGTGCGAAGGCTAGAAACCAGTATTTCTTCTTGT 7800

Qy      3183 LysThrSerLeuGlnArgValGlnLeuHisIleAlaMetPheGlnTrpGlnHisGluAsp 3202
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7801 AAGACAAGCCTGCAGCGGGTTCAGCTGCATATTGCCATGTTTCAGTGGCAACATGAAGAT 7860

Qy      3203 LeuLeuIleAsnArgProGlnAlaMetSerValThrProProProArgSerAlaIleLeu 3222
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7861 CTACTTATCAATAGACCACAAGCCATGTCAGTCACACCTCCCCCACGGTCTGCTATCCTA 7920

Qy      3223 ThrSerMetLysLysLysLeuHisThrLeuSerGlnIleGluThrSerIleAlaThrVal 3242
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7921 ACCAGCATGAAAAAGAAGCTGCATACCCTGAGCCAGATTGAAACTTCTATTGCGACAGTT 7980

Qy      3243 GlnGluLysLeuAlaAlaLeuGluSerSerIleGluGlnArgLeuLysTrpAlaGlyGly 3262
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      7981 CAGGAGAAGCTAGCTGCACTTGAATCAAGTATTGAACAGCGACTCAAGTGGGCAGGTGGT 8040

Qy      3263 AlaAsnProAlaLeuAlaProValLeuGlnAspPheGluAlaThrIleAlaGluArgArg 3282
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      8041 GCCAACCCTGCATTGGCCCCTGTACTACAAGATTTTGAAGCAACGATAGCTGAAAGAAGA 8100

Qy      3283 AsnLeuValLeuLysGluSerGlnArgAlaSerGlnValThrPheLeuCysSerAsnIle 3302
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      8101 AATCTTGTCCTTAAAGAGAGCCAAAGAGCAAGTCAGGTCACATTTCTCTGCAGCAATATC 8160

Qy      3303 IleHisPheGluSerLeuArgThrArgThrAlaGluAlaLeuAsnLeuAspAlaAlaLeu 3322
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      8161 ATTCATTTTGAAAGTTTACGAACAAGAACTGCAGAAGCCTTAAACCTGGATGCGGCGTTA 8220

Qy      3323 PheGluLeuIleLysArgCysGlnGlnMetCysSerPheAlaSerGlnPheAsnSerSer 3342
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      8221 TTTGAACTAATCAAGCGATGTCAGCAGATGTGTTCGTTTGCATCACAGTTTAACAGTTCA 8280

Qy      3343 ValSerGluLeuGluLeuArgLeuLeuGlnArgValAspThrGlyLeuGluHisProIle 3362
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      8281 GTGTCTGAGTTAGAGCTTCGTTTATTACAGAGAGTGGACACTGGTCTTGAACATCCTATT 8340

Qy      3363 GlySerSerGluTrpLeuLeuSerAlaHisLysGlnLeuThrGlnAspMetSerThrGln 3382
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      8341 GGCAGCTCTGAATGGCTTTTGTCAGCACACAAACAGTTGACCCAGGATATGTCTACTCAG 8400

Qy      3383 ArgAlaIleGlnThrGluLysGluGlnGlnIleGluThrValCysGluThrIleGlnAsn 3402
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      8401 AGGGCAATTCAGACAGAGAAAGAGCAGCAGATAGAAACGGTCTGTGAAACAATTCAGAAT 8460

Qy      3403 LeuValAspAsnIleLysThrValLeuThrGlyHisAsnArgGlnLeuGlyAspValLys 3422
```

```
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8461 CTGGTTGATAATATAAAGACTGTGCTCACTGGTCATAACCGACAGCTTGGAGATGTCAAA 8520

Qy       3423 HisLeuLeuLysAlaMetAlaLysAspGluGluAlaAlaLeuAlaAspGlyGluAspVal 3442
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8521 CATCTCTTGAAAGCTATGGCTAAGGATGAAGAAGCTGCTCTGGCAGATGGTGAAGATGTT 8580

Qy       3443 ProTyrGluAsnSerValArgGlnPheLeuGlyGluTyrLysSerTrpGlnAspAsnIle 3462
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8581 CCCTATGAGAACAGTGTTAGGCAGTTTTTGGGTGAATATAAATCATGGCAAGACAACATT 8640

Qy       3463 GlnThrValLeuPheThrLeuValGlnAlaMetGlyGlnValArgSerGlnGluHisVal 3482
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8641 CAAACAGTTCTATTTACATTAGTCCAGGCTATGGGTCAGGTTCGAAGTCAAGAACACGTT 8700

Qy       3483 GluMetLeuGlnGluIleThrProThrLeuLysGluLeuLysThrGlnSerGlnSerIle 3502
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8701 GAAATGCTCCAGGAAATCACTCCCACCTTGAAAGAACTGAAAACACAAAGTCAGAGTATC 8760

Qy       3503 TyrAsnAsnLeuValSerPheAlaSerProLeuValThrAspAlaThrAsnGluCysSer 3522
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8761 TATAATAATTTAGTGAGTTTTGCATCACCCTTAGTCACCGATGCAACAAATGAATGTTCG 8820

Qy       3523 SerProThrSerSerAlaThrTyrGlnProSerPheAlaAlaAlaValArgSerAsnThr 3542
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8821 AGTCCAACGTCATCTGCTACTTATCAGCCATCCTTCGCTGCAGCAGTCCGGAGTAACACT 8880

Qy       3543 GlyGlnLysThrGlnProAspValMetSerGlnAsnAlaArgLysLeuIleGlnLysAsn 3562
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8881 GGCCAGAAGACTCAGCCTGATGTCATGTCACAGAATGCTAGAAAGCTGATCCAGAAAAAT 8940

Qy       3563 LeuAlaThrSerAlaAspThrProProSerThrValProGlyThrGlyLysSerValAla 3582
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       8941 CTTGCTACATCAGCTGATACTCCACCAAGCACCGTTCCAGGAACTGGCAAGAGTGTTGCT 9000

Qy       3583 CysSerProLysLysAlaValArgAspProLysThrGlyLysAlaValGlnGluArgAsn 3602
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       9001 TGTAGTCCTAAAAAGGCAGTCAGAGACCCTAAAACTGGGAAAGCGGTGCAAGAGAGAAAC 9060

Qy       3603 SerTyrAlaValSerValTrpLysArgValLysAlaLysLeuGluGlyArgAspValAsp 3622
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       9061 TCCTATGCAGTGAGTGTGTGGAAGAGAGTGAAAGCCAAGTTAGAGGGCCGAGATGTTGAT 9120

Qy       3623 ProAsnArgArgMetSerValAlaGluGlnValAspTyrValIleLysGluAlaThrAsn 3642
                 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       9121 CCGAATAGGAGGATGTCAGTTGCTGAACAGGTTGACTATGTCATTAAGGAAGCAACTAAT 9180

Qy       3643 LeuAspAsnLeuAlaGlnLeuTyrGluGlyTrpThrAlaTrpVal 3657
                 ||||||||||||||||||||||||||||||||||||||||||||
Db       9181 CTAGATAACTTGGCTCAGCTGTATGAAGGTTGGACAGCCTGGGTG 9225
```

APPENDIX B

```
Q96Q15_HUMAN
ID   Q96Q15_HUMAN PRELIMINARY;      PRT;  3657 AA.
AC   Q96Q15;
DT   01-DEC-2001 (TrEMBLrel. 19, Created)
DT   01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT   01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DE   Phosphatidylinositol 3-kinase-related protein kinase.
GN   Name=smg-1;
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae;
OC   Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RX   MEDLINE=21429078; PubMed=11544179; DOI=10.1101/gad.913001;
RA   Yamashita A., Ohnishi T., Kashima I., Taya Y., Ohno S.;
RT   "Human SMG-1, a novel phosphatidylinositol 3-kinase-related protein
RT   kinase, associates with components of the mRNA surveillance complex
RT   and is involved in the regulation of nonsense-mediated mRNA decay.";
RL   Genes Dev. 15:2215-2228(2001).
DR   EMBL; AB061371; BAB70696.1; -; mRNA.
DR   Ensembl; ENSG00000157106; Homo sapiens.
DR   GO; GO:0005488; F:binding; IEA.
DR   GO; GO:0016301; F:kinase activity; IEA.
DR   GO; GO:0016773; F:phosphotransferase activity, alcohol group . . .; IEA.
DR   InterPro; IPR011989; ARM-like.
DR   InterPro; IPR003152; FATC.
DR   InterPro; IPR000357; HEAT.
DR   InterPro; IPR000403; PI3/4_kinase_cat.
DR   Pfam; PF02260; FATC; 1.
DR   Pfam; PF02985; HEAT; 1.
DR   Pfam; PF00454; PI3_PI4_kinase; 1.
DR   SMART; SM00146; PI3Kc; 1.
DR   PROSITE; PS00916; PI3_4_KINASE_2; 1.
DR   PROSITE; PS50290; PI3_4_KINASE_3; 1.
KW   Kinase.
SQ   SEQUENCE   3657 AA;  410286 MW;  182D59966FD82243 CRC64;

  Query Match            100.0%;  Score 18745;  DB 2;  Length 3657;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches 3657;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MSRRAPGSRLSSGGTNYSRSWNDWQPRTDSASADPGNLKYSSSRDRGGSSSYGLQPSNSA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSRRAPGSRLSSGGTNYSRSWNDWQPRTDSASADPGNLKYSSSRDRGGSSSYGLQPSNSA 60

Qy         61 VVSRQRHDDTRVHADIQNDEKGGYSVNGGSGENTYGRKSLGQELRVNNVTSPEFTSVQHG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 VVSRQRHDDTRVHADIQNDEKGGYSVNGGSGENTYGRKSLGQELRVNNVTSPEFTSVQHG 120

Qy        121 SRALATKDMRKSQERSMSYSDESRLSNLLRRITREDDRDRRLATVKQLKEFIQQPENKLV 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 SRALATKDMRKSQERSMSYSDESRLSNLLRRITREDDRDRRLATVKQLKEFIQQPENKLV 180

Qy        181 LVKQLDNILAAVHDVLNESSKLLQELRQEGACCLGLLCASLSYEAEKIFKWIFSKFSSSA 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 LVKQLDNILAAVHDVLNESSKLLQELRQEGACCLGLLCASLSYEAEKIFKWIFSKFSSSA 240

Qy        241 KDEVKLLYLCATYKALETVGEKKAFSSVMQLVMTSLQSILENVDTPELLCKCVKCILLVA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 KDEVKLLYLCATYKALETVGEKKAFSSVMQLVMTSLQSILENVDTPELLCKCVKCILLVA 300

Qy        301 RCYPHIFSTNFRDTVDILVGWHIDHTQKPSLTQQVSGWLQSLEPFWVADLAFSTTLLGQF 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 RCYPHIFSTNFRDTVDILVGWHIDHTQKPSLTQQVSGWLQSLEPFWVADLAFSTTLLGQF 360

Qy        361 LEDMEAYAEDLSHVASGESVDEDVPPPSVSLPKLAALLRVFSTVVRSIGERFSPIRGPPI 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 LEDMEAYAEDLSHVASGESVDEDVPPPSVSLPKLAALLRVFSTVVRSIGERFSPIRGPPI 420
```

```
Qy        421 TEAYVTDVLYRVMRCVTAANQVFFSEAVLTAANECVGVLLGSLDPSMTIHCDMVITYGLD 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TEAYVTDVLYRVMRCVTAANQVFFSEAVLTAANECVGVLLGSLDPSMTIHCDMVITYGLD 480

Qy        481 QLENCQTCGTDYIISVLNLLTLIVEQINTKLPSSFVEKLFIPSSKLLFLRYHKEKEVVAV 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 QLENCQTCGTDYIISVLNLLTLIVEQINTKLPSSFVEKLFIPSSKLLFLRYHKEKEVVAV 540

Qy        541 AHAVYQAVLSLKNIPVLETAYKLILGEMTCALNNLLHSLQLPEACSEIKHEAFKNHVFNV 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 AHAVYQAVLSLKNIPVLETAYKLILGEMTCALNNLLHSLQLPEACSEIKHEAFKNHVFNV 600

Qy        601 DNAKFVVKFDLSALTTIGNAKNSLIGMWALSPTVFALLSKNLMIVHSDLAVHFPAIQYAV 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 DNAKFVVKFDLSALTTIGNAKNSLIGMWALSPTVFALLSKNLMIVHSDLAVHFPAIQYAV 660

Qy        661 LYTLYSHCTRHDHFISSSLSSASPSLFDGAVISTVTTATKKHFSIILNLLGILLKKDNLN 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 LYTLYSHCTRHDHFISSSLSSASPSLFDGAVISTVTTATKKHFSIILNLLGILLKKDNLN 720

Qy        721 QDTRKLLMTWALEAAVLMRKSETYAPLFSLPSFHKFCKGLLANTLVEDVNICLQACSSLH 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 QDTRKLLMTWALEAAVLMRKSETYAPLFSLPSFHKFCKGLLANTLVEDVNICLQACSSLH 780

Qy        781 ALSSSLPDDLLQRCVDVCRVQLVHSGTRIRQAFGKLLKSIPLDVVLSNNNHTEIQEISLA 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 ALSSSLPDDLLQRCVDVCRVQLVHSGTRIRQAFGKLLKSIPLDVVLSNNNHTEIQEISLA 840

Qy        841 LRSHMSKAPSNTFHPQDFSDVISFILYGNSHRTGKDNWLERLFYSCQRLDKRDQSTIPRN 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 LRSHMSKAPSNTFHPQDFSDVISFILYGNSHRTGKDNWLERLFYSCQRLDKRDQSTIPRN 900

Qy        901 LLKTDAVLWQWAIWEAAQFTVLSKLRTPLGRAQDTFQTIEGIIRSLAAHTLNPDQDVSQW 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 LLKTDAVLWQWAIWEAAQFTVLSKLRTPLGRAQDTFQTIEGIIRSLAAHTLNPDQDVSQW 960

Qy        961 TTADNDEGHGNNQLRLVLLLQYLENLEKLMYNAYEGCANALTSPPKVIRTFFYTNRQTCQ 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 TTADNDEGHGNNQLRLVLLLQYLENLEKLMYNAYEGCANALTSPPKVIRTFFYTNRQTCQ 1020

Qy       1021 DWLTRIRLSIMRVGLLAGQPAVTVRHGFDLLTEMKTTSLSQGNELEVTIMMVVEALCELH 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 DWLTRIRLSIMRVGLLAGQPAVTVRHGFDLLTEMKTTSLSQGNELEVTIMMVVEALCELH 1080

Qy       1081 CPEAIQGIAVWSSSIVGKNLLWINSVAQQAEGRFEKASVEYQEHLCAMTGVDCCISSFDK 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 CPEAIQGIAVWSSSIVGKNLLWINSVAQQAEGRFEKASVEYQEHLCAMTGVDCCISSFDK 1140

Qy       1141 SVLTLANAGRNSASPKHSLNGESRKTVLSKPTDSSPEVINYLGNKACEFYISIADWAAVQ 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 SVLTLANAGRNSASPKHSLNGESRKTVLSKPTDSSPEVINYLGNKACEFYISIADWAAVQ 1200

Qy       1201 EWQNAIHDLKKSTSSTSLNLKADFNYIKSLSSFESGKFVECTEQLELLPGENINLLAGGS 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 EWQNAIHDLKKSTSSTSLNLKADFNYIKSLSSFESGKFVECTEQLELLPGENINLLAGGS 1260

Qy       1261 KEKIDMKKLLPNMLSPDPRELQKSIEVQLLRSSVCLATALNPIEQDQKWQSITENVVKYL 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 KEKIDMKKLLPNMLSPDPRELQKSIEVQLLRSSVCLATALNPIEQDQKWQSITENVVKYL 1320

Qy       1321 KQTSRIAIGPLRLSTLTVSQSLPVLSTLQLYCSSALENTVSNRLSTEDCLIPLFSEALRS 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 KQTSRIAIGPLRLSTLTVSQSLPVLSTLQLYCSSALENTVSNRLSTEDCLIPLFSEALRS 1380

Qy       1381 CKQHDVRPWMQALRYTMYQNQLLEKIKEQTVPIRSHLMELGLTAAKFARKRGNVSLATRL 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 CKQHDVRPWMQALRYTMYQNQLLEKIKEQTVPIRSHLMELGLTAAKFARKRGNVSLATRL 1440

Qy       1441 LAQCSEVQLGKTTTAQDLVQHFKKLSTQGQVDEKWGPELDIEKTKLLYTAGQSTHAMEML 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 LAQCSEVQLGKTTTAQDLVQHFKKLSTQGQVDEKWGPELDIEKTKLLYTAGQSTHAMEML 1500
```

```
Qy       1501 SSCAISFCKSVKAEYAVAKSILTLAKWIQAEWKEISGQLKQVYRAQHQQNFTGLSTLSKN 1560
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 SSCAISFCKSVKAEYAVAKSILTLAKWIQAEWKEISGQLKQVYRAQHQQNFTGLSTLSKN 1560

Qy       1561 ILTLIELPSVNTMEEEYPRIESESTVHIGVGEPDFILGQLYHLSSVQAPEVAKSWAALAS 1620
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 ILTLIELPSVNTMEEEYPRIESESTVHIGVGEPDFILGQLYHLSSVQAPEVAKSWAALAS 1620

Qy       1621 WAYRWGRKVVDNASQGEGVRLLPREKSEVQNLLPDTITEEEKERIYGILGQAVCRPAGIQ 1680
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 WAYRWGRKVVDNASQGEGVRLLPREKSEVQNLLPDTITEEEKERIYGILGQAVCRPAGIQ 1680

Qy       1681 DEDITLQITESEDNEEDDMVDVIWRQLISSCPWLSELDESATEGVIKVWRKVVDRIFSLY 1740
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 DEDITLQITESEDNEEDDMVDVIWRQLISSCPWLSELDESATEGVIKVWRKVVDRIFSLY 1740

Qy       1741 KLSCSAYFTFLKLNAGQIPLDEDDPRLHLSHRVEQSTDDMIVMATLRLLRLLVKHAGELR 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 KLSCSAYFTFLKLNAGQIPLDEDDPRLHLSHRVEQSTDDMIVMATLRLLRLLVKHAGELR 1800

Qy       1801 QYLEHGLETTPTAPWRGIIPQLFSRLNHPEVYVRQSICNLLCRVAQDSPHLILYPAIVGT 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 QYLEHGLETTPTAPWRGIIPQLFSRLNHPEVYVRQSICNLLCRVAQDSPHLILYPAIVGT 1860

Qy       1861 ISLSSESQASGNKFSTAIPTLLGNIQGEELLVSECEGGSPPASQDSNKDEPKSGLNEDQA 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 ISLSSESQASGNKFSTAIPTLLGNIQGEELLVSECEGGSPPASQDSNKDEPKSGLNEDQA 1920

Qy       1921 MMQDCYSKIVDKLSSANPTMVLQVQMLVAELRRVTVLWDELWLGVLLQQHMYVLRRIQQL 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 MMQDCYSKIVDKLSSANPTMVLQVQMLVAELRRVTVLWDELWLGVLLQQHMYVLRRIQQL 1980

Qy       1981 EDEVKRVQNNNTLRKEEKIAIMRERHTALMKPIVFALEHVRSITAAPAETPHEKWFQDNY 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 EDEVKRVQNNNTLRKEEKIAIMRERHTALMKPIVFALEHVRSITAAPAETPHEKWFQDNY 2040

Qy       2041 GDAIENALEKLKTPLNPAKPGSSWIPFKEIMLSLQQRAQKRASYILRLEEISPWLAAMTN 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 GDAIENALEKLKTPLNPAKPGSSWIPFKEIMLSLQQRAQKRASYILRLEEISPWLAAMTN 2100

Qy       2101 TEIALPGEVSARDTVTIHSVGGTITILPTKTKPKKLLFLGSDGKSYPYLFKGLEDLHLDE 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 TEIALPGEVSARDTVTIHSVGGTITILPTKTKPKKLLFLGSDGKSYPYLFKGLEDLHLDE 2160

Qy       2161 RIMQFLSIVNTMFATINRQETPRFHARHYSVTPLGTRSGLIQWVDGATPLFGLYKRWQQR 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 RIMQFLSIVNTMFATINRQETPRFHARHYSVTPLGTRSGLIQWVDGATPLFGLYKRWQQR 2220

Qy       2221 EAALQAQKAQDSYQTPQNPGIVPRPSELYYSKIGPALKTVGLSLDVSRRDWPLHVMKAVL 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 EAALQAQKAQDSYQTPQNPGIVPRPSELYYSKIGPALKTVGLSLDVSRRDWPLHVMKAVL 2280

Qy       2281 EELMEATPPNLLAKELWSSCTTPDEWWRVTQSYARSTAVMSMVGYIIGLGDRHLDNVLID 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 EELMEATPPNLLAKELWSSCTTPDEWWRVTQSYARSTAVMSMVGYIIGLGDRHLDNVLID 2340

Qy       2341 MTTGEVVHIDYNVCFEKGKSLRVPEKVPFRMTQNIETALGVTGVEGVFRLSCEQVLHIMR 2400
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2341 MTTGEVVHIDYNVCFEKGKSLRVPEKVPFRMTQNIETALGVTGVEGVFRLSCEQVLHIMR 2400

Qy       2401 RGRETLLTLLEAFVYDPLVDWTAGGEAGFAGAVYGGGGQQAESKQSKREMEREITRSLFS 2460
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2401 RGRETLLTLLEAFVYDPLVDWTAGGEAGFAGAVYGGGGQQAESKQSKREMEREITRSLFS 2460

Qy       2461 SRVAEIKVNWFKNRDEMLVVLPKLDGSLDEYLSLQEQLTDVEKLQGKLLEEIEFLEGAEG 2520
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2461 SRVAEIKVNWFKNRDEMLVVLPKLDGSLDEYLSLQEQLTDVEKLQGKLLEEIEFLEGAEG 2520

Qy       2521 VDHPSHTLQHRYSEHTQLQTQQRAVQEAIQVKLNEFEQWITHYQAAFNNLEATQLASLLQ 2580
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2521 VDHPSHTLQHRYSEHTQLQTQQRAVQEAIQVKLNEFEQWITHYQAAFNNLEATQLASLLQ 2580
```

```
Qy       2581 EISTQMDLGPPSYVPATAFLQNAGQAHLISQCEQLEGEVGALLQQRRSVLRGCLEQLHHY 2640
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2581 EISTQMDLGPPSYVPATAFLQNAGQAHLISQCEQLEGEVGALLQQRRSVLRGCLEQLHHY 2640

Qy       2641 ATVALQYPKAIFQKHRIEQWKTWMEELICNTTVERCQELYRKYEMQYAPQPPPTVCQFIT 2700
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2641 ATVALQYPKAIFQKHRIEQWKTWMEELICNTTVERCQELYRKYEMQYAPQPPPTVCQFIT 2700

Qy       2701 ATEMTLQRYAADINSRLIRQVERLKQEAVTVPVCEDQLKEIERCIKVFLHENGEEGSLSL 2760
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2701 ATEMTLQRYAADINSRLIRQVERLKQEAVTVPVCEDQLKEIERCIKVFLHENGEEGSLSL 2760

Qy       2761 ASVIISALCTLTRRNLMMEGAASSAGEQLVDLTSRDGAWFLEELCSMSGNVTCLVQLLKQ 2820
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2761 ASVIISALCTLTRRNLMMEGAASSAGEQLVDLTSRDGAWFLEELCSMSGNVTCLVQLLKQ 2820

Qy       2821 CHLVPQDLDIPNPMEASETVHLANGVYTSLQELNSNFRQIIFPEALRCLMKGEYTLESML 2880
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2821 CHLVPQDLDIPNPMEASETVHLANGVYTSLQELNSNFRQIIFPEALRCLMKGEYTLESML 2880

Qy       2881 HELDGLIEQTTDGVPLQTLVESLQAYLRNAAMGLEEETHAHYIDVARLLHAQYGELIQPR 2940
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2881 HELDGLIEQTTDGVPLQTLVESLQAYLRNAAMGLEEETHAHYIDVARLLHAQYGELIQPR 2940

Qy       2941 NGSVDETPKMSAGQMLLVAFDGMFAQVETAFSLLVEKLNKMEIPIAWRKIDIIREARSTQ 3000
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2941 NGSVDETPKMSAGQMLLVAFDGMFAQVETAFSLLVEKLNKMEIPIAWRKIDIIREARSTQ 3000

Qy       3001 VNFFDDDNHRQVLEEIFFLKRLQTIKEFFRLCGTFSKTLSGSSSLEDQNTVNGPVQIVNV 3060
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3001 VNFFDDDNHRQVLEEIFFLKRLQTIKEFFRLCGTFSKTLSGSSSLEDQNTVNGPVQIVNV 3060

Qy       3061 KTLFRNSCFSEDQMAKPIKAFTADFVRQLLIGLPNQALGLTLCSFISALGVDIIAQVEAK 3120
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3061 KTLFRNSCFSEDQMAKPIKAFTADFVRQLLIGLPNQALGLTLCSFISALGVDIIAQVEAK 3120

Qy       3121 DFGAESKVSVDDLCKKAVEHNIQIGKFSQLVMNRATVLASSYDTAWKKHDLVRRLETSIS 3180
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3121 DFGAESKVSVDDLCKKAVEHNIQIGKFSQLVMNRATVLASSYDTAWKKHDLVRRLETSIS 3180

Qy       3181 SCKTSLQRVQLHIAMFQWQHEDLLINRPQAMSVTPPPRSAILTSMKKKLHTLSQIETSIA 3240
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3181 SCKTSLQRVQLHIAMFQWQHEDLLINRPQAMSVTPPPRSAILTSMKKKLHTLSQIETSIA 3240

Qy       3241 TVQEKLAALESSIEQRLKWAGGANPALAPVLQDFEATIAERRNLVLKESQRASQVTFLCS 3300
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3241 TVQEKLAALESSIEQRLKWAGGANPALAPVLQDFEATIAERRNLVLKESQRASQVTFLCS 3300

Qy       3301 NIIHFESLRTRTAEALNLDAALFELIKRCQQMCSFASQFNSSVSELELRLLQRVDTGLEH 3360
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3301 NIIHFESLRTRTAEALNLDAALFELIKRCQQMCSFASQFNSSVSELELRLLQRVDTGLEH 3360

Qy       3361 PIGSSEWLLSAHKQLTQDMSTQRAIQTEKEQQIETVCETIQNLVDNIKTVLTGHNRQLGD 3420
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3361 PIGSSEWLLSAHKQLTQDMSTQRAIQTEKEQQIETVCETIQNLVDNIKTVLTGHNRQLGD 3420

Qy       3421 VKHLLKAMAKDEEAALADGEDVPYENSVRQFLGEYKSWQDNIQTVLFTLVQAMGQVRSQE 3480
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3421 VKHLLKAMAKDEEAALADGEDVPYENSVRQFLGEYKSWQDNIQTVLFTLVQAMGQVRSQE 3480

Qy       3481 HVEMLQEITPTLKELKTQSQSIYNNLVSFASPLVTDATNECSSPTSSATYQPSFAAAVRS 3540
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3481 HVEMLQEITPTLKELKTQSQSIYNNLVSFASPLVTDATNECSSPTSSATYQPSFAAAVRS 3540

Qy       3541 NTGQKTQPDVMSQNARKLIQKNLATSADTPPSTVPGTGKSVACSPKKAVRDPKTGKAVQE 3600
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3541 NTGQKTQPDVMSQNARKLIQKNLATSADTPPSTVPGTGKSVACSPKKAVRDPKTGKAVQE 3600

Qy       3601 RNSYAVSVWKRVKAKLEGRDVDPNRRMSVAEQVDYVIKEATNLDNLAQLYEGWTAWV 3657
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3601 RNSYAVSVWKRVKAKLEGRDVDPNRRMSVAEQVDYVIKEATNLDNLAQLYEGWTAWV 3657
```

APPENDIX C

US-09-417-822-2
; Sequence 2, Application US/09417822
; Patent No. 6344549
; GENERAL INFORMATION:
; APPLICANT: Keegan, Kathy
; TITLE OF INVENTION: ATR-2
; FILE REFERENCE: 27866/35633
; CURRENT APPLICATION NUMBER: US/09/417,822
; CURRENT FILING DATE: 1999-10-14
; NUMBER OF SEQ ID NOS: 43
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 2
; LENGTH: 2930
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-417-822-2

Query Match 80.1%; Score 15023; DB 2; Length 2930;
Best Local Similarity 99.9%; Pred. No. 0;
Matches 2927; Conservative 2; Mismatches 1; Indels 0; Gaps 0;

```
Qy        728 MTWALEAAVLMRKSETYAPLFSLPSFHKFCKGLLANTLVEDVNICLQACSSLHALSSSLP 787
              ||||||||||:||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MTWALEAAVLMKKSETYAPLFSLPSFHKFCKGLLANTLVEDVNICLQACSSLHALSSSLP 60

Qy        788 DDLLQRCVDVCRVQLVHSGTRIRQAFGKLLKSIPLDVVLSNNNHTEIQEISLALRSHMSK 847
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 DDLLQRCVDVCRVQLVHSGTRIRQAFGKLLKSIPLDVVLSNNNHTEIQEISLALRSHMSK 120

Qy        848 APSNTFHPQDFSDVISFILYGNSHRTGKDNWLERLFYSCQRLDKRDQSTIPRNLLKTDAV 907
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 APSNTFHPQDFSDVISFILYGNSHRTGKDNWLERLFYSCQRLDKRDQSTIPRNLLKTDAV 180

Qy        908 LWQWAIWEAAQFTVLSKLRTPLGRAQDTFQTIEGIIRSLAAHTLNPDQDVSQWTTADNDE 967
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 LWQWAIWEAAQFTVLSKLRTPLGRAQDTFQTIEGIIRSLAAHTLNPDQDVSQWTTADNDE 240

Qy        968 GHGNNQLRLVLLLQYLENLEKLMYNAYEGCANALTSPPKVIRTFFYTNRQTCQDWLTRIR 1027
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 GHGNNQLRLVLLLQYLENLEKLMYNAYEGCANALTSPPKVIRTFFYTNRQTCQDWLTRIR 300

Qy       1028 LSIMRVGLLAGQPAVTVRHGFDLLTEMKTTSLSQGNELEVTIMMVVEALCELHCPEAIQG 1087
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 LSIMRVGLLAGQPAVTVRHGFDLLTEMKTTSLSQGNELEVTIMMVVEALCELHCPEAIQG 360

Qy       1088 IAVWSSSIVGKNLLWINSVAQQAEGRFEKASVEYQEHLCAMTGVDCCISSFDKSVLTLAN 1147
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 IAVWSSSIVGKNLLWINSVAQQAEGRFEKASVEYQEHLCAMTGVDCCISSFDKSVLTLAN 420

Qy       1148 AGRNSASPKHSLNGESRKTVLSKPTDSSPEVINYLGNKACEFYISIADWAAVQEWQNAIH 1207
              |||||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||
Db        421 AGRNSASPKHSLNGESRKTVLSKPTDSSPEVINYLGNKACECYISIADWAAVQEWQNAIH 480

Qy       1208 DLKKSTSSTSLNLKADFNYIKSLSSFESGKFVECTEQLELLPGENINLLAGGSKEKIDMK 1267
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 DLKKSTSSTSLNLKADFNYIKSLSSFESGKFVECTEQLELLPGENINLLAGGSKEKIDMK 540

Qy       1268 KLLPNMLSPDPRELQKSIEVQLLRSSVCLATALNPIEQDQKWQSITENVVKYLKQTSRIA 1327
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 KLLPNMLSPDPRELQKSIEVQLLRSSVCLATALNPIEQDQKWQSITENVVKYLKQTSRIA 600

Qy       1328 IGPLRLSTLTVSQSLPVLSTLQLYCSSALENTVSNRLSTEDCLIPLFSEALRSCKQHDVR 1387
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 IGPLRLSTLTVSQSLPVLSTLQLYCSSALENTVSNRLSTEDCLIPLFSEALRSCKQHDVR 660

Qy       1388 PWMQALRYTMYQNQLLEKIKEQTVPIRSHLMELGLTAAKFARKRGNVSLATRLLAQCSEV 1447
```

```
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 PWMQALRYTMYQNQLLEKIKEQTVPIRSHLMELGLTAAKFARKRGNVSLATRLLAQCSEV 720

Qy       1448 QLGKTTTAQDLVQHFKKLSTQGQVDEKWGPELDIEKTKLLYTAGQSTHAMEMLSSCAISF 1507
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 QLGKTTTAQDLVQHFKKLSTQGQVDEKWGPELDIEKTKLLYTAGQSTHAMEMLSSCAISF 780

Qy       1508 CKSVKAEYAVAKSILTLAKWIQAEWKEISGQLKQVYRAQHQQNFTGLSTLSKNILTLIEL 1567
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 CKSVKAEYAVAKSILTLAKWIQAEWKEISGQLKQVYRAQHQQNFTGLSTLSKNILTLIEL 840

Qy       1568 PSVNTMEEEYPRIESESTVHIGVGEPDFILGQLYHLSSVQAPEVAKSWAALASWAYRWGR 1627
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 PSVNTMEEEYPRIESESTVHIGVGEPDFILGQLYHLSSVQAPEVAKSWAALASWAYRWGR 900

Qy       1628 KVVDNASQGEGVRLLPREKSEVQNLLPDTITEEEKERIYGILGQAVCRPAGIQDEDITLQ 1687
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 KVVDNASQGEGVRLLPREKSEVQNLLPDTITEEEKERIYGILGQAVCRPAGIQDEDITLQ 960

Qy       1688 ITESEDNEEDDMVDVIWRQLISSCPWLSELDESATEGVIKVWRKVVDRIFSLYKLSCSAY 1747
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 ITESEDNEEDDMVDVIWRQLISSCPWLSELDESATEGVIKVWRKVVDRIFSLYKLSCSAY 1020

Qy       1748 FTFLKLNAGQIPLDEDDPRLHLSHRVEQSTDDMIVMATLRLLRLLVKHAGELRQYLEHGL 1807
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 FTFLKLNAGQIPLDEDDPRLHLSHRVEQSTDDMIVMATLRLLRLLVKHAGELRQYLEHGL 1080

Qy       1808 ETTPTAPWRGIIPQLFSRLNHPEVYVRQSICNLLCRVAQDSPHLILYPAIVGTISLSSES 1867
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 ETTPTAPWRGIIPQLFSRLNHPEVYVRQSICNLLCRVAQDSPHLILYPAIVGTISLSSES 1140

Qy       1868 QASGNKFSTAIPTLLGNIQGEELLVSECEGGSPPASQDSNKDEPKSGLNEDQAMMQDCYS 1927
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 QASGNKFSTAIPTLLGNIQGEELLVSECEGGSPPASQDSNKDEPKSGLNEDQAMMQDCYS 1200

Qy       1928 KIVDKLSSANPTMVLQVQMLVAELRRVTVLWDELWLGVLLQQHMYVLRRIQQLEDEVKRV 1987
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 KIVDKLSSANPTMVLQVQMLVAELRRVTVLWDELWLGVLLQQHMYVLRRIQQLEDEVKRV 1260

Qy       1988 QNNNTLRKEEKIAIMRERHTALMKPIVFALEHVRSITAAPAETPHEKWFQDNYGDAIENA 2047
                ||||||||||||||||:||||||||||||||||||||||||||||||||||||||||||||||||
Db       1261 QNNNTLRKEEKIAIMREKHTALMKPIVFALEHVRSITAAPAETPHEKWFQDNYGDAIENA 1320

Qy       2048 LEKLKTPLNPAKPGSSWIPFKEIMLSLQQRAQKRASYILRLEEISPWLAAMTNTEIALPG 2107
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1321 LEKLKTPLNPAKPGSSWIPFKEIMLSLQQRAQKRASYILRLEEISPWLAAMTNTEIALPG 1380

Qy       2108 EVSARDTVTIHSVGGTITILPTKTKPKKLLFLGSDGKSYPYLFKGLEDLHLDERIMQFLS 2167
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1381 EVSARDTVTIHSVGGTITILPTKTKPKKLLFLGSDGKSYPYLFKGLEDLHLDERIMQFLS 1440

Qy       2168 IVNTMFATINRQETPRFHARHYSVTPLGTRSGLIQWVDGATPLFGLYKRWQQREAALQAQ 2227
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1441 IVNTMFATINRQETPRFHARHYSVTPLGTRSGLIQWVDGATPLFGLYKRWQQREAALQAQ 1500

Qy       2228 KAQDSYQTPQNPGIVPRPSELYYSKIGPALKTVGLSLDVSRRDWPLHVMKAVLEELMEAT 2287
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1501 KAQDSYQTPQNPGIVPRPSELYYSKIGPALKTVGLSLDVSRRDWPLHVMKAVLEELMEAT 1560

Qy       2288 PPNLLAKELWSSCTTPDEWWRVTQSYARSTAVMSMVGYIIGLGDRHLDNVLIDMTTGEVV 2347
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1561 PPNLLAKELWSSCTTPDEWWRVTQSYARSTAVMSMVGYIIGLGDRHLDNVLIDMTTGEVV 1620

Qy       2348 HIDYNVCFEKGKSLRVPEKVPFRMTQNIETALGVTGVEGVFRLSCEQVLHIMRRGRETLL 2407
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1621 HIDYNVCFEKGKSLRVPEKVPFRMTQNIETALGVTGVEGVFRLSCEQVLHIMRRGRETLL 1680
```

```
Qy       2408 TLLEAFVYDPLVDWTAGGEAGFAGAVYGGGGQQAESKQSKREMEREITRSLFSSRVAEIK 2467
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1681 TLLEAFVYDPLVDWTAGGEAGFAGAVYGGGGQQAESKQSKREMEREITRSLFSSRVAEIK 1740

Qy       2468 VNWFKNRDEMLVVLPKLDGSLDEYLSLQEQLTDVEKLQGKLLEEIEFLEGAEGVDHPSHT 2527
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1741 VNWFKNRDEMLVVLPKLDGSLDEYLSLQEQLTDVEKLQGKLLEEIEFLEGAEGVDHPSHT 1800

Qy       2528 LQHRYSEHTQLQTQQRAVQEAIQVKLNEFEQWITHYQAAFNNLEATQLASLLQEISTQMD 2587
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1801 LQHRYSEHTQLQTQQRAVQEAIQVKLNEFEQWITHYQAAFNNLEATQLASLLQEISTQMD 1860

Qy       2588 LGPPSYVPATAFLQNAGQAHLISQCEQLEGEVGALLQQRRSVLRGCLEQLHHYATVALQY 2647
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1861 LGPPSYVPATAFLQNAGQAHLISQCEQLEGEVGALLQQRRSVLRGCLEQLHHYATVALQY 1920

Qy       2648 PKAIFQKHRIEQWKTWMEELICNTTVERCQELYRKYEMQYAPQPPPTVCQFITATEMTLQ 2707
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1921 PKAIFQKHRIEQWKTWMEELICNTTVERCQELYRKYEMQYAPQPPPTVCQFITATEMTLQ 1980

Qy       2708 RYAADINSRLIRQVERLKQEAVTVPVCEDQLKEIERCIKVFLHENGEEGSLSLASVIISA 2767
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1981 RYAADINSRLIRQVERLKQEAVTVPVCEDQLKEIERCIKVFLHENGEEGSLSLASVIISA 2040

Qy       2768 LCTLTRRNLMMEGAASSAGEQLVDLTSRDGAWFLEELCSMSGNVTCLVQLLKQCHLVPQD 2827
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2041 LCTLTRRNLMMEGAASSAGEQLVDLTSRDGAWFLEELCSMSGNVTCLVQLLKQCHLVPQD 2100

Qy       2828 LDIPNPMEASETVHLANGVYTSLQELNSNFRQIIFPEALRCLMKGEYTLESMLHELDGLI 2887
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2101 LDIPNPMEASETVHLANGVYTSLQELNSNFRQIIFPEALRCLMKGEYTLESMLHELDGLI 2160

Qy       2888 EQTTDGVPLQTLVESLQAYLRNAAMGLEEETHAHYIDVARLLHAQYGELIQPRNGSVDET 2947
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2161 EQTTDGVPLQTLVESLQAYLRNAAMGLEEETHAHYIDVARLLHAQYGELIQPRNGSVDET 2220

Qy       2948 PKMSAGQMLLVAFDGMFAQVETAFSLLVEKLNKMEIPIAWRKIDIIREARSTQVNFFDDD 3007
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2221 PKMSAGQMLLVAFDGMFAQVETAFSLLVEKLNKMEIPIAWRKIDIIREARSTQVNFFDDD 2280

Qy       3008 NHRQVLEEIFFLKRLQTIKEFFRLCGTFSKTLSGSSSLEDQNTVNGPVQIVNVKTLFRNS 3067
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2281 NHRQVLEEIFFLKRLQTIKEFFRLCGTFSKTLSGSSSLEDQNTVNGPVQIVNVKTLFRNS 2340

Qy       3068 CFSEDQMAKPIKAFTADFVRQLLIGLPNQALGLTLCSFISALGVDIIAQVEAKDFGAESK 3127
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2341 CFSEDQMAKPIKAFTADFVRQLLIGLPNQALGLTLCSFISALGVDIIAQVEAKDFGAESK 2400

Qy       3128 VSVDDLCKKAVEHNIQIGKFSQLVMNRATVLASSYDTAWKKHDLVRRLETSISSCKTSLQ 3187
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2401 VSVDDLCKKAVEHNIQIGKFSQLVMNRATVLASSYDTAWKKHDLVRRLETSISSCKTSLQ 2460

Qy       3188 RVQLHIAMFQWQHEDLLINRPQAMSVTPPPRSAILTSMKKKLHTLSQIETSIATVQEKLA 3247
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2461 RVQLHIAMFQWQHEDLLINRPQAMSVTPPPRSAILTSMKKKLHTLSQIETSIATVQEKLA 2520

Qy       3248 ALESSIEQRLKWAGGANPALAPVLQDFEATIAERRNLVLKESQRASQVTFLCSNIIHFES 3307
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2521 ALESSIEQRLKWAGGANPALAPVLQDFEATIAERRNLVLKESQRASQVTFLCSNIIHFES 2580

Qy       3308 LRTRTAEALNLDAALFELIKRCQQMCSFASQFNSSVSELELRLLQRVDTGLEHPIGSSEW 3367
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2581 LRTRTAEALNLDAALFELIKRCQQMCSFASQFNSSVSELELRLLQRVDTGLEHPIGSSEW 2640

Qy       3368 LLSAHKQLTQDMSTQRAIQTEKEQQIETVCETIQNLVDNIKTVLTGHNRQLGDVKHLLKA 3427
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2641 LLSAHKQLTQDMSTQRAIQTEKEQQIETVCETIQNLVDNIKTVLTGHNRQLGDVKHLLKA 2700
```

```
Qy       3428 MAKDEEAALADGEDVPYENSVRQFLGEYKSWQDNIQTVLFTLVQAMGQVRSQEHVEMLQE 3487
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2701 MAKDEEAALADGEDVPYENSVRQFLGEYKSWQDNIQTVLFTLVQAMGQVRSQEHVEMLQE 2760

Qy       3488 ITPTLKELKTQSQSIYNNLVSFASPLVTDATNECSSPTSSATYQPSFAAAVRSNTGQKTQ 3547
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2761 ITPTLKELKTQSQSIYNNLVSFASPLVTDATNECSSPTSSATYQPSFAAAVRSNTGQKTQ 2820

Qy       3548 PDVMSQNARKLIQKNLATSADTPPSTVPGTGKSVACSPKKAVRDPKTGKAVQERNSYAVS 3607
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2821 PDVMSQNARKLIQKNLATSADTPPSTVPGTGKSVACSPKKAVRDPKTGKAVQERNSYAVS 2880

Qy       3608 VWKRVKAKLEGRDVDPNRRMSVAEQVDYVIKEATNLDNLAQLYEGWTAWV 3657
             ||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2881 VWKRVKAKLEGRDVDPNRRMSVAEQVDYVIKEATNLDNLAQLYEGWTAWV 2930
```